THESIS

FOR THE AWARD OF DEGREE OF

DOCTOR OF MEDICINE

SESSION 2020-2023

HISTOPATHOLOGICAL STUDY OF ENDOMETRIAL BIOPSIES IN ABNORMAL UTERINE BLEEDING

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ACKNOWLEDGEMENT

I express my deep sense of gratitude and indebtedness to my most respected guide and teacher, Dr. Malay Bajpai, Professor, Department of Pathology, Santosh Medical College and Hospital, Ghaziabad for his constant help, valuable advice, inspirational demeanor and able guidance throughout the study. His ever-willing keenness to help and guide was a constant source of inspiration to me.

I heartily thank Dr. Swati Singh, Associate Professor, Department of Pathology, Santosh Medical College and Hospital, Ghaziabad for her help, valuable advice and suggestions.

I would also like to thank Dr. Mayurika Tyagi, Associate Professor, Department of Pathology, Santosh Medical College and Hospital, Ghaziabad for her help and support.

I would like to thank all my family members for constantly supporting me and encouraging me.

I thank the ever-helpful postgraduates and all the technical and non-technical staff members of the department for their help.

I am grateful to Dr. Alka Agrawal, Dean, Santosh Medical College and Hospital, Ghaziabad.

Last, but not the least, I would like to express my love and thanks to my friend Dr. Arushi Agarwal, Dr. Aarthi K.B and Karan Yadav for being there for me always.

Above all, I thank the Almighty and all the patients without whom this study would not have been possible.

LIST OF ABBREVIATIONS

AUB Abnormal Uterine Bleeding

DUB Dysfunctional Uterine Bleeding

IUCD Intrauterine Contraceptive Device

OPD Outpatient Department

WHO World Health Organization

D&C Dilatation And Curettage

FSH Follicular Stimulating Hormone

Gnrh Gonadotropin Releasing Hormone

H&E Hematoxylin And Eosin

HCG Human Chorionic Gonadotropin

VEGF Vascular Endothelial Growth Factor

HMB Heavy Menstrual Bleeding

LH Luteinizing Hormone

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INTRODUCTION

Any uterine bleeding that is larger than normal, lasts longer, and varies in regularity or frequency is considered abnormal uterine bleeding (AUB). Changes in menstruation frequency, duration of flow, or amount of blood loss are all signs of abnormal uterine bleeding.[1] AUB is responsible for over 30% of all gynaecological outpatient attendance.[2]

Abnormal uterine bleeding (AUB) refers to uterine bleeding caused by both organic and non-organic causes. In other words, "abnormal uterine bleeding is the most prevalent presenting symptom and primary gynaecological problem, accounting for up to one-third of all outpatient gynaecological visits." [3, 4]

AUB (abnormal uterine bleeding) is a common reason for women of all ages to see a gynaecologist. Uterine haemorrhage can be caused by both organic and non-organic factors. After medical explanations for irregular uterine bleeding have been ruled out, endometrial biopsy or curettage could be a safe and useful diagnostic step.[5]

A bleeding pattern that differs in frequency, length, and amount from that found during a normal menstrual cycle or after menopause is known as abnormal uterine bleeding.[6] Menorrhagia, metrorrhagia, polymenorrhoea, metromenorrhagia, perimenorrhagia, and postmenopausal bleeding are all examples of abnormal uterine bleeding. Abnormal uterine bleeding is a frequent condition that affects people of all ages and has a variety of reasons. A multitude of illnesses can cause it. It may result from a pathological process that is not directly related to the uterus, such as hyper-androgenic an ovulation in patients with polycystic ovaries, hypothalamic dysfunction, hyperprolactinemia, hypothyroidism, pituitary disease, premature ovarian failure, or iatrogenic causes like radiation or chemotherapy.[7]

A woman's quality of life is harmed by abnormal uterine bleeding. Information on age and menstrual history, as well as a clinical examination, are required to assess endometrial samples. Endometrial curettage, which is performed to obtain material for histological study to aid in diagnosis and management, cannot be overstated, particularly in the peri-menopausal and post-menopausal age ranges.

It's possible that abnormal uterine bleeding is caused by structural or functional issues. Fibroids, polyps, endometrial hyperplasia, and endometrial cancer are some of the most common structural reasons.[8]

It is most commonly connected with anovulatory menstrual cycles. Adolescence and perimenopausal women are especially vulnerable. The gold standard for determining the origin of endometrial cancer is histopathological evaluation of endometrial biopsies and

curetting.[9,10]

In terms of endometrial dating, it's also crucial when examining patients for infertility. Its histological appearance is utilised to track ovulation and determine hormonal health. Endometrial biopsy was chosen to assess DUB because it is a safe, relatively simple procedure that may be completed as a day-care procedure.[5]

Endometrial polyps, retention of gestational products, chronic endometritis, infectious disorders, uterine cancer, myoma of the uterus, ovarian and tube tumours, and trophoblastic diseases are all organic causes of irregular uterine bleeding.[11]

Other tests, such as hormonal assays, are more expensive, and hormonal assay laboratories may not be available in rural regions.[7]

Uterine bleeding in women of childbearing age that is not due to organic factors falls into a broad category known as dysfunctional uterine bleeding (DUB). DUB is defined as abnormal uterine bleeding accompanied by a functional problem rather than an endometrial or uterine pathological pathology.[6,7]

Dysfunctional uterine bleeding (DUB) is a subtype of AUB that encompasses non-organic reasons of irregular bleeding. It's found in half of the women who have AUB. When there is abnormal uterine bleeding, an endometrial biopsy is routinely performed to rule out organic pathology. Because the etiologies of abnormal uterine bleeding change depending on age and menstrual status, age and menstrual history are particularly essential.[5] Pregnancy problems, including termination, are more likely in women of reproductive age, whereas atrophy and organic diseases are more common in postmenopausal women.[11]

Dysfunctional uterine bleeding results from derangement in the magnitude or duration of hormone effects mainly oestrogen and progesterone on the endometrium. The functional condition can only be diagnosed once structural, iatrogenic, pharmacological, psychiatric, and systemic problems have been ruled out using a variety of procedures.[12]

Only after a histological study has ruled out organic reasons can a diagnosis of Dysfunctional Uterine Bleeding be made. In DUB, there are three common patterns. The first is known as "oestrogen breakthrough bleeding," which occurs when a "persistent follicle" produces oestrogen continuously. The proliferating endometrium develops to the point where it outgrows its own blood supply, resulting in breakthrough bleeding. The second is "oestrogen withdrawl bleeding," which is caused by a "failed follicle," in which the follicle generates less oestrogen than usual.[13] Both of these conditions are linked to anovulation. Due to follicular or luteal phase abnormalities, the third finding is "ovulatory endometrium."

The typical cyclical physiological changes that occur in the endometrium of women during the reproductive period are controlled by the ovaries' cyclical release of oestrogen and progesterone.[8,9] During the menstrual cycle, the concentration of receptors for these hormones likewise varies cyclically. Hyperplasias and endometrial malignancies, particularly type I, express oestrogen and progesterone receptors. The levels of these receptors can provide crucial prognostic information. They also provide details on the suitability of hormone therapy.

The key element in the development of Dysfunctional Uterine Bleeding is hormonal imbalance. A combination of histological and immunohistochemical assessment of the endometrium allows for a better understanding of this change.[10]

The protocol for handling any endometrial sampling material is determined by the clinical indication for the specimen submission, which may be for evaluation of infertility or preparation for In Vitro Fertilization (IVF), evaluation of abnormal uterine bleeding, or follow-up of a previous cytological or histological diagnosis.[4] The endometrium, which may be the site of a primary or secondary tumour, can be examined as part of a hysterectomy specimen.

Based on the patient's age and medical history, DUB cases may have structural or functional causes. In several research, endometrial biopsies were most frequently performed due to infertility, and secretory phase endometrium was the most frequently observed morphologic type.[7,8]

Similar investigations found a low frequency of tuberculous endometritis and endometrial cancer. Other investigations found endometrial hyperplasia to be the most common morphological feature, as well as a significant number of cases of endometritis, albeit it was unclear whether endometrial culture was performed in these cases. In other investigations, endometrial hyperplasia, an intraepithelial nonneoplastic proliferative lesion, was found to peak during the perimenopausal and menopausal periods, with a varied incidence.[10,11,12]

Endometrial polyps were discovered to be the most common structural cause of abnormal uterine bleeding, among other things, and were especially important in patients who were considering IVF.

Without a solid diagnosis, many women with unexplained uterine bleeding may undergo unnecessary hysterectomy. Endometrial sample could be a useful initial step in diagnosing irregular uterine bleeding. In order to establish effective care, accurate diagnosis of the causal factor of irregular uterine bleeding in any age range is critical.[4]

The gold standard diagnostic technique for abnormal uterine bleeding is histopathological investigation of submitted endometrial tissue.[4,5] Furthermore, a thorough histological evaluation aids in the development of effective treatment plans. Histopathological diagnosis varies by age, with endometrial hyperplasia and cancer being more common in peri- and postmenopausal women, while hormonal alterations appear to be more common in younger age groups.[6]

Therefore, light microscopy examination of histological characteristics of endometrial samples remains the gold standard for clinical diagnosis of endometrial pathology.[9] The clinical differential diagnosis varies by age group, therefore histological evaluation of endometrial curettage material aids in the diagnosis of disease presenting with abnormal uterine bleeding.[14]

REVIEW OF LITERATURE

Bleeding from the Secretory endometrium following an ovulatory cycle is characterized as the term "Normal Menstruation". Generally, menstruation happens in an average interval of 28days with a blood loss of approximately 35ml (20-80 ml) and it lasts for >= 5days [15]. However, anyuterine bleeding with larger volume, greater duration, and irregular in frequency of the cycle is termed as "abnormal uterine bleeding". On the other hand, abnormal uterine bleeding without any association or relation with any of the general genital tract abnormalities and/or endocrinological diseases is termed as "dysfunctional uterine bleeding".

The term Heavy Menstrual Bleeding (HMB) is used when bleeding interferes with the woman's quality of life in physical, emotional, social and maternal aspects. Women of all age groups present to the gynaecologist with abnormal uterine bleeding. AUB occurs in 9-14% of women of reproductive, perimenopausal and postmenopausal age groups. It significantly impairs the quality of life and increases financial burden.

General Physiology of Normal Menstruation:

Any bleeding not fulfilling the requirements of normal menstruation is termed as "Abnormal uterine bleeding" [16].

The hypothalamo-pituitary-ovarian axis is healthy if a woman has a regular monthly period. Menstrual irregularities result from any place along the axis interruption.[17] Therefore, it is essential to understand the physiology of the menstrual cycle.

There is only one released oocyte per menstrual cycle. The secretory phase follows this. The secretory endometrium sheds after a fixed interval of 14 days following ovulation. Monthly menstruation is how this shows up. Endometrial shedding ends after an egg is fertilised and an embryo is implanted.

Menstrual Cycle:

Throughout the reproductive stage of life, cyclical menstruation continues with an average rhythm with a frequency of 4-6 days of bleeding included (except pregnancy and lactation). It can often be divided into two cycles, which are as follows:

- The menstrual cycle
- The endometrial Cycle

Ovarian cycle:

One follicle grows and matures during this cycle. The remainder of the cells form the corpus luteum once it ovulates.

This can be broken down into three stages, including

- Follicular Stage 1
- Ovulation Stage 2
- Luteal Stage 3

The phase of the follicle:

The first phase of the ovarian cycle is now. The follicle stimulating hormone released from the pituitary stimulates the follicle which matures as a result. Under the influence of several hormonal autocrine and paracrine inter loops only one follicle develops, while all others stop developing. Through the progressive stages of primordial, preantral, antral, and preovulatory graffian follicle, this dominant follicle will continue to develop. The phrase "tertiary (Grafian) follicle" refers to the completely developed follicle. The ovum is located in this follicle. This period typically lasts 14 days, however its duration varies.

The period of ovulation:

A mature ovum is released from the ovarian follicle during ovulation. LH surges from the anterior pituitary when oestrogen levels in the late follicular phase are sustained at their peak for 24-48 hours (positive feedback effect). This procedure may begin on the average cycle's 12th day and last up to 48 hours. Under the influence of LH, the egg matures and the follicular wall weakens.

As a result, the secondary oocyte is released from the fully formed follicle. The secondary oocyte, which develops into a mature ovum, gives rise to ootidis.

Luteal Phase:

After the ovum is released from the follicle, this phase begins. There, the ca interna cells and the maiming granulosa develop into lutein cells that enlarge and gather lipid inclusions. They seem yellowish as a result. This mass is known as the corpus luteum. The typical duration is 14 days.

This time spans from the corpus luteum's death (down in serum levels of estradiol, inhibin, and progesterone) until the choice of a dominant follicle for the following cycle.

Distinct phases of the menstrual cycle involve different hormones, which can be detected in hormones. They include:

- The follicular stimulating hormone (FSH)
- The hormone lutinizing (LH)
- Estrogen
- Progestrone

ENDOMETRIAL CYCLE

The lining epithelium of the uterine cavity above the level of the internals is called the endometrium. It is made up of stroma, blood vessels, glands, and surface epithelium. An organ where intricate interactions between the immunological, endocrine, and circulatory systems occur is the endometrium (18). wherein there are established to be two separate divisions. It's them,

- Basal zone (Stratum Basalis) as first and
- Second as Functional Zone

BASAL ZONE:

It is nourished by the basal arteries and makes up around one-third of the endometrium's overall depth. In this zone, no cyclic changes are seen. From this zone, all of the components regenerate. Itmeasuresabout1mm.

FUNCTIONAL ZONE:

Estrogen and progesterone, two cyclic ovarian hormones, have an impact on this region. Tradition has it that an ovulatory cycle goes through four stages as various components change.

- Phase 1: The regeneration stage
- Phase 2: The Proliferation stage
- Phase 3: The Secretory stage
- Phase 4: The Menstruation stage

The stromal cells and the epithelial cells multiply when estrogens, which the ovary secretes in increasing amounts during the first phase of the cycle, are present. In a 28-day cycle, this phase lasts from the fifth to the fourteenth day.

It is about one-third of the total depth of the endometrium, supplied by the basal arteries uninfluenced by hormone. No cyclic changes are observed in this zone. The regeneration of all the components occurs from this zone. It measures about 1mm. The average endometrial thickness is 2-3 mm.

PROLIFERATION PHASE:

The regenerated epithelium is thin during this stage. The epithelial mitoses are present in the short, narrow glands. The stromal cells exhibit mitosis as well (stromal cells are stellate or spindle shaped).[19]

(8 to 10 days) MID DAYS:

The glands are long and curved. The lining epithelium is columnar and frequently undergoes mitoses along with varying stromal edema.

LATE DAYS (between 11 and 14 days):

There are tortuous glands. Observed nuclear pseudo stratification. The stroma is actively developing and relatively thick.

SECRETORY PHASE:

The combined effects of oestrogen and progesterone released from the corpus luteum after ovulation are to blame for the alterations in the components. Therefore, progesterone can only affect an endometrium that has already been stimulated by oestrogen. The secretory phase lasts a fixed amount of time, 14 days. This results from the corpus luteum precisely and rhythmically involuting following ovulation. At this stage, the endometrial thickness is at its thickest (6–8 mm).

A transitional period lasts from day 14 until day 15. After ovulation, no obvious changes are visible for 36–48 hours.[19]

Early Secretory Period (16 to 20 days):

This phase is characterised by pronounced glandular alterations. Sub nuclear vacuoles start to form by day 16. Around day 17, regular vacuolation starts to occur. The size of vacuoles starts to shrink around day 18. Early secretions flood the lumen, and the nucleus has reached the base of the cell. Few vacuoles are still present by day 19 and intraluminal secretions are visible. Mitoses and pseudo stratification are absent. Intraluminal secretions found maximum on day 20.

Mid to Late Secretory Phase (21 to 27 days):

In this phase, stromal changes are noticeable. There are many levels of secretory fatigue seen. There is noticeable stromal edoema on day 21. The peak of the stromal edoema, or "naked nuclei," occurs on day 22. On the 23rd day, spiral arteries are noticeable and periarteriolar predecidual alteration is discovered. Predecidual alteration is noticeable on day 24 and stromal mitoses resume. Predecidual differentiation begins on the 25th day beneath the superficial epithelium, and granular lymphocytes multiply. Pre decidua begins to confluence on the 26th day. Granular lymphocytes reach their peak on day 27. Confluent predecidua sheets form, along with localised necrosis. Secretory fatigue of glands is visible between 24 and 27 days. The intraluminal tufts on the glands give them a saw-toothed appearance. The glands are tortuous.

MESTRUAL ENDOMETRIUM:

One constant feature of the premenstrual phase is the regression of the corpus luteum, which is accompanied by a drop in oestrogen and progesterone levels. Endometrial glands and stroma are destroyed. By the end of the 28th day, this is noticeable throughout the functional layer. Additionally, fibrin thrombi form in tiny vessels. Condensed and crumpled with necrotic debris is the stroma. Also evident is neutrophilic infiltration (20). This inflammation is entirely natural and well controlled.[21] 0.5 mm thick is the endometrium.

REGENERATION:

The endometrium begins to regenerate just before menstruation stops and is finished two to three days later. Re-growing is the stromal ground material. The endometrium is about 2 mm thick.[22]

ENDOMETRIAL ANGIOGENESIS:

The only tissue in the body that cycles through rapid growth and loss is the endometrium. A careful balance between elements that encourage and restrict blood vessel growth is necessary for endometrial angiogenesis. Progesterone and estradiol regulate angiogenesis by promoting or repressing growth factors. Both of these hormones increase VEGF (vascular endothelial growth factor) synthesis, which aids in the formation of endometrial arteries. Thrombo spondin-1, which is in charge of preventing the proliferation of blood vessels during the secretory phase, is stimulated by progesterone. When oestrogen and progesterone are removed from the body, proteolytic enzymes are released into the extracellular matrix. These enzymes damage the arteries and matrix, causing menstrual shedding.[23]

DEFINITIONS:

Menorrhagia (hypermenorrhea):

Excessive bleeding that lasts longer than seven days and is more than 80 mL in volume.

Polymenorrhea

The cycles more frequently than once every 21 days and continues to do so. Epimenorrhagia or polymenorrhagia are the terms used to describe an increase in the amount and duration of bleeding that is related.

Metrorrhagia:

Inconsistent cycles can show up as contact bleeding or intermenstrual bleeding.

Menometrorrhagia:

This phrase is used when bleeding is so irregular and heavy that it is impossible to identify the menstrual phase at all.

Oligomenorrhea:

Cyclical bleeding that happens regularly but over a long period of time (more than 35 days).

Hypomennorhea:

When a woman's period bleeds abnormally little and for fewer than two days.

Bleeding between periods:

This describes bruising that takes place in between otherwise regular menstrual cycles but is typically not extensive.

Abrupt onset of menstruation:

A term used to describe menstruation that occurs before the age of 10 years.

Posy coital bleeding:

Denotes vaginal bleeding after sexual intercourse.

EFFECTS OF STEROID HORMONES ON THE ENDOMETRIUM:

Progesterone and oestrogen are sex steroids made from cholesterol. The ovaries are primarily where progesterone and testosterone are first created. In order to activate aromatase, FSH operates on the granulosa cells of the ovary. Progesterone and testosterone are converted into estrogens by this enzyme. The main and strongest oestrogen that is released by the ovaries is -estradiol.

After puberty, the size of the uterus rises two to three times, but the changes that estrogens cause in the uterine endometrium are more significant than the increase in uterus size. The endometrial stroma's ability to proliferate is increased by this hormone. The endometrial glands also grow fully. The implanted ovum benefits from this in terms of nutrition.

Endometrial atrophy is caused by extremely low oestrogen levels, whereas excessive oestrogen levels cause hyperplasia.

Estrogen receptors are located in the nucleus. The ER and ER subtypes of oestrogen receptors

exist. Two genes, ESR1 for ER and ESR2 for ER, are responsible for encoding these receptors. The female genital tract contains the most ER-1, whereas the prostate and ovaries have the most ER-1 expression.

The cytoplasm and the nucleus both contain oestrogen receptors. However, estrogen's significant actions are controlled by its interaction with nuclear receptors. Chaperones are a wide family of proteins that are associated with oestrogen receptors. These proteins separate when oestrogen enters the cell and begins to bind with the receptors. The dimerization of the receptors happens after oestrogen binds to them. The oestrogen sensitive elements in the target genes are then bound by dimers.

Endometrial cancer prognosis is determined by the quantity of oestrogen and progesterone receptors in the body. Patients with higher levels of these receptors live longer than those with lower levels of receptors. According to Liao et al., if the tumour was receptor positive, the prognosis was dramatically enhanced even for patients who had lymph node metastases. At least for the ER, the absolute number of receptors may be significant; the higher the level, the better the prognosis. PR appears to be a stronger predictor of survival than ER.[24]

ENDOMETRIAL SAMPLING TECHNIQUES:

DILATATION AND CURETTAGE (D&C)

The most frequent procedure on women has been diagnostic curettage for many years. The method has several restrictions, though. Cervical dilatation is uncomfortable, thus there are dangers related to the required general anaesthetic as well. These hazards include bleeding, infection, and uterine perforation.

ENDOTRACHEAL BIOPSY

A single endometrium strip can be removed without a cervical dilatation or a general anaesthesia as an outpatient operation. Rarely is this approach applied.

BRAZILIAN ASPIRATIOR:

This suction curette device has an opening on one side of its bent tip made of a steel can with a 3–4 mm diameter. The endometrial tissue is extracted using suction and a syringe that is attached. This process captures different amounts of data.

PIPELLE BIOPSY:

In the United States and Europe, this is likely the most popular outpatient procedure for sampling the endometrial cavity. This short process results in significantly less pain than Novak curette or Vabra aspirator. The diagnostic precision of the Pipelle biopsy is comparable to that of the Vabra aspirator, but producing less tissue. Although some studies have revealed a poor pick-up rate for early, low-volume tumours, it is no less reliable than other methods for detecting endometrial cancer.

ENDOMETRIAL RESULT:

One of the various techniques for endometrial ablation involves trans cervical resection of the endometrium. It is used to treat abnormal uterine haemorrhage conservatively. Only after hyperplasia and cancer have been ruled out using other sampling techniques like hysteroscopic biopsy or D&C should this be done. The endometrium needs to be hormonally suppressed before this treatment. My metrical tissue makes up the majority of the tissue that was retrieved. However, this method cannot be used to accurately identify adenomyosis.

ADEQUACY OF SPECIMEN:

Pathologists commonly deal with a sparse specimen due to the widespread use of methods like pipelle biopsy. In late proliferative, late secretory, hyperplasias, and carcinomas, a sufficient sample is frequently obtained. Postmenopausal trophies frequently have thin specimens. However, a poor biopsy sample cannot completely rule out hyperplasia or carcinoma, as cases have been documented where a subsequent hysterectomy revealed malignancy despite a poor biopsy sample.

If only a small amount of tissue is found, the biopsy need not be repeated. Even if only a tiny bit of endometrial tissue is present, the specimen can still be considered sufficient. When a sparse tissue is present, it is best to use the phrase unassessable rather than inadequate. Endometrial specimens were divided into "unassessable" and "inadequate" categories by Mc Cluggage (scant tissue is present). Since there is no difference in the ultimate clinical diagnosis between the two categories, this classification is not particularly important.[25] Before doing a repeat biopsy in such circumstances, the results of other tests including ultrasound and hysteroscopy should be taken into consideration. D&C should be performed if the clinical symptoms and other examinations indicate some pathology.[26]

AGE-GRADED CAUSES OF ABNORMAL UTERINE BLEEDING:

In 2011, FIGO coined the term "Abnormal Uterine Bleeding" to refer to all abnormal uterine bleeding, whether or not there is an organic lesion present.

Pre-puberty **:** Precocious puberty (hypothalamic, pituitary or ovarian origin)

Adolescence **:** An ovulatory cycle

Reproductive age **:** Complications of pregnancy (abortion, ectopic pregnancy)

Peri-menopause : Irregular shedding, organic lesions (carcinoma, hyperplasia, polyps) irregular shedding, organic lesions (carcinoma, hyperplasia, polyps)

Post-menopause-organic lesions (carcinoma, hyperplasia, polyps),
endometrial atrophy.

The newer classification system is known by the acronym **PALM–COEIN** [27].

CLASSIFICATION OF AUB:

Contrary to the PALM group, the COEIN group cannot be detected by imaging and histopathology.

CLASSIFICATION OF AUB (FIGO - 2011)			
Structural causes (PALM)		**Non-structural systemic causes (COEIN)**	
Polyp	AUB-P	Coagulopathy	AUB-C
Adenomyosis	AUB-A	Ovulatory dysfunction	AUB-O
Leiomyoma - Sub mucosal myoma - Other myoma	AUB-LAUB-L SMAUB-LO	Endometrial	AUB-E
Malignancy and hyperplasia	AUB-M	Iatrogenic	AUB-I
		Not yet identified	AUB-N

The PALM group includes 4 causes that can be detected by imaging or histopathology, whereas the COEIN group includes causes that cannot be detected by these modalities [28].

Polyp (AUB-P)

Polyps can be detected by ultrasound, hysteroscopy or histopathology. They can be sub divided onthe basis of number, size, location and histology.

Adenomyosis (AUB-A)

It can be diagnosed by ultrasound or MRI. It is further sub divided on the basis of the depth of myometrial invasion. Most often, it is asymptomatic and an incidental finding in hysterectomy specimens.

Leiomyoma (AUB-L)

Leiomyomas usually are not the cause of abnormal uterine bleeding. Mostly they are

incidental findings. Myomas that are causal in abnormal bleeding usually involve the uterine cavity. Theyare further sub divided into primary, secondary and tertiary groups based on their number, sizeand location.

Malignancy and pre-malignant lesions:

It is rare in reproductive age group. In this age group, it occurs usually in the setting of polycystic ovarian disease and chronic anovulation. Diagnosis is made by histopathological examination of the endometrium (D/C, biopsy).

Coagulopathy (AUB-C)

Coagulopathies are the cause of AUB in 13% to 20% of women in the reproductive age group.

The most common cause is Von Wille brand's disease.

Ovulatory disorders (AUB-O)

Ovulatory disorders are the cause of AUB in 20% of cases. These are the result of "Luteal–out– of–phase" events (LOOP) with deficient progesterone. Hypothyroid is hyper prolactinoma are other causes.

Endometrial causes (AUB-E)

Endometrium normally produces prostaglandins from arachidonic acid, which is a fatty acid. Of these, PGE2 and PGI2 are vasodilators and anti-platelet aggregates. PGF2a and thromboxane A2 cause vasoconstriction and platelet aggregates. Progesterone is responsible for the secretion of PGF 2a. In an ovulatory cycle, the absence of progesterone and thereby of PGF 2a causesmenorrhagia. Rare endometrial causes of AUB include tuberculous endometritis and infection, especially chlamydia.

Iatrogenic (AUB-I)

It is caused by steroidal hormones administered as oral contraceptives or IUCD. Copper T may cause "break-through bleeding" or menorrhagia. Other drugs causing abnormal bleeding include anticoagulants, phenothiazines and tricyclic anti-depressants.

Not-classified (AUB-N)

This includes rare causes like arterio venousmal formations, varicose veins of uterine vessels, myohyperplasia and cases for which no cause can be identified by routine investigations.

AUB CAN BE ACUTE OR CHRONIC

Acute bleeding-may occur sporadically (denovo) or may be super imposed on chronic AUB, and requires immediate treatment.

Chronic AUB – Abnormal menstrual bleeding related to volume, timing, regularity and duration of bleeding that lasts for 6 months (minimum 3 months), and requires thorough investigations.

DYSFUNCTIONAL UTERINE BLEEDING

The term Dysfunctional Uterine Bleeding is used once the organic causes of abnormal bleedinghas been excluded. Upto 50% of women with abnormal bleeding have DUB [29]. DUB can be classified into

1. Ovulatory – 10 to 20%
2. Anovulatory – 80 to 90%

OVULATORY BLEEDING

Ovular bleeding can present as either polymenorrhea or menorrhagia.

POLYMENORRHEA

It usually occurs following childbirth and abortion, during adolescence and premenopausal period,and in pelvic inflammatory disease. This is due to shortening of follicular phase due to hyperstimulation by FSH or premature lysis of the corpus luteum. Endometrial study prior to or within few hours of menstruation reveals secretory changes.

Menorrhagia Two types are seen Irregular shedding of the endometrium

This is due to incomplete and slow degeneration of the corpus luteum (Halban's

disease). Endometrial sampling performed after 5th or 6th day of the onset of menstruation reveals a mixture of secretory and proliferative endometrium.

IRREGULAR RIPENING OF THE ENDOMETRIUM

This is due to the poor formation and function of the corpus luteum. Endometrial study prior to or soon after spotting reveals patchy areas of secretory changes amidst proliferative endometrium.

ANOVULATORY UTERINE BLEEDING

Continued exposure to estrogen in the presence of anovulation leads to marked endometrialproliferation. After a certain extent, the endometrium cannot support the proliferation and shedding occurs called as "an ovulatory shedding". This should be differentiated from the normal menstrual shedding. The absence of secretory exhaustion and presence of fibrin clots distinguishesan ovulatory shedding from menstrual endometrium. Also, in anovulation the glands lose their uniformity in size, shape and distribution leading to a pattern called disordered proliferative endometrium. It also leads to cystic dilatation of the glands and tubal metaplasia (30). The underlying cause is unknown. Presumably, the failure of ovulation reflects an abnormal gonadotrophin stimulus.

METROPATHIA HAEMORRHAGICA

It is a specialized form of anovulatory AUB, seen in women between 40and 45 years. The basic fault may lie in the ovaries or may be due to a disturbance of the rhythmic secretion of the gonadotropins. There is a slow increase in the secretion of estrogen but no negative feedback inhibition of FSH. The net effect is a gradual rise in the level of estrogen with a concomitant phaseof amenorrhea for about 6–8 weeks. After a variable period, however, the estrogen level falls resulting in the endometrial shedding with heavy bleeding. Histopathology shows thick endometrium with polypoidal projections. There is cystic glandular hyperplasia. Some of the glands are small, others are large giving the appearance of "Swiss cheese" pattern.

SPECIFIC CAUSES OF ABNORMAL UTERINE BLEEDING ENDOMETRITIS

Endometritis commonly occurs in the reproductive age group. It usually presents with abnormal uterine bleeding. Predisposing factors include recent pregnancy, prior instrumentation, intrauterinedevices and cervical stenosis. Endometritis may also coexist with polyps, fibroid, hyperplasia or endometrial carcinoma. The endometrium shows proliferative activity and glandular architectural distortion. There is surface break down similar to that seen in menstrual break down. In lowpower, the stromal cells show spindle appearance.

In acute endometritis, the predominant inflammatory cells are neutrophils, sometimes seen within the glandular lumina forming micro abscesses. The characteristic finding of endometritis is the presence of plasma cells. Other inflammatory cells like neutrophils and lymphocytes can be present in normal endometrium. In chronic endometritis, lymphocytes are prominent sometimes forming lymphoid follicles. Endometrial surface and glandular epithelium may show metaplastic changes. Immunohistochemistry using VS38 or Syndecan can be used to differentiate plasma cellsfrom the endometrial stromal cells, which resembles plasma cells. Plasma cells show positivity to

both the markers whereas stromal cells positive for only VS38.

EFFECTS OF EXOGENOUS HORMONAL AGENTS AND DRUGS

A wide variety of hormonal agents are used in women for various indications. The effects of the most common hormonal agents used are discussed below.

ESTROGEN ONLY HORMONE REPLACEMENT THERAPY

These are rarely used in women because of the risk of endometrial hyperplasia and adeno carcinoma. The morphological features include proliferative activity similar to disordered proliferation, endometrial hyperplasia or endometrioid adeno carcinoma. The risk of carcinoma increases with the dose and length of treatment and the adeno carcinoma which develops is usually of a nearly stage and low-grade.

COMBINED ESTROGEN AND PROGESTIN HORMONE THERAPY

Combined therapy is preferred in women with uterus due to the disadvantages of estrogen only therapy [12]. Estrogen and progestin combination may be given sequentially or simultaneously (continuously). In sequential therapy, the endometrium shows weakly proliferative activity during estrogen therapy and poorly develops secretory activity during progestin therapy. This regimen doesn't completely abolish the risk of carcinoma and the risk of endometrial hyperplasia with sequential regimen is 5.4%. With continuous combined regimen, the endometrium shows atrophy or weak secretory activity.

This regimen reduces the risk of development of endometrial hyperplasia and carcinoma. Hence continuous combined regimen is preferred to sequential HRT in perimenopausal women and post- menopausal women.

PROGESTIN – ONLY COMPOUNDS

These are commonly prescribed for abnormal uterine bleeding, endometriosis, contraception and for endometrial protection in patients taking tamoxifen. They usually result in endometrial atrophywith predecidual changes or decidualization of the stroma.

GONADOTROPHIN RELEASING HORMONE AGONISTS

These are usually used in the management of uterine fibroids and endometriosis. The continuous administration of Gn RH agonists results in decreased production of FSH and LH thereby causing decreased production of estrogen by the ovaries. This results in shrinkage of uterine leiomyomas. The endometrium shows atrophy or weak proliferative activity.

ANDROGENS

These are used in the treatment of endometriosis, as HRT, menorrhagia and endometrial hyperplasia. The endometrium has weak secretory activity during the initial phase of treatment but with continued treatment, the endometrium shows atrophic changes.

AIMS AND OBJECTIVES

AIM: The aim of the study is to assess the histopathology of endometrium for identifying the causes of abnormal uterine bleeding among different age groups and to find out endometrial carcinoma in perimenopausal and postmenopausal women.

OBJECTIVES:

1. To evaluate histopathology of endometrium for identifying the causes of abnormaluterine bleeding.
2. To observe the incidence of various pathology in different age group.
3. To rule out endometrial carcinoma in perimenopausal and postmenopausal women.

MATERIALS AND METHODS

METHODOLOGY

Study Design

The study design was observational cross-sectional.

Place of study and sample frame:

This study was conducted at Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh and the sample will be received from Obstetrics and Gynaecology department.

Period of study

The study was conducted according to the sample size.

Study population

Women in all age groups attending Department of Obstetrics and Gynaecology (OBGY) OPD/IPD with abnormal uterine bleeding**.**

Sample size

A total of 130 specimens of endometrium (endometrial curetting's/biopsy hysterectomy specimens) will be taken for this study.

Sample Size Determination

$$n = \frac{Z^2_{\frac{\alpha}{2}} * P * Q}{l^2}$$

where, P = Proportion of endometrial hyperplasia among abnormal uterine bleeding is 42.4% (Reference article: Bhat R, Sudhamani S, Roplekar P. Histopathological study of endometrium in abnormaluterine bleeding in perimenopausal andpostmenopausal women. J Sci Soc 2019; 46:95-8) [31].

Q = 1-P = 57.6% L = 20 % (Relative precision or error)i.e., 20% of 42.4% (Prevalence) Then, n = 130 Therefore, the sample size will be 130 as study samples.

Inclusion criteria

Women of all age group attending Department of Obstetrics and Gynaecology (OBGY) OPD/IPD withabnormal uterine bleeding.

Exclusion criteria

1. Patients with organic lesions involving the genital tract like leiomyomas, adenomyosis, cervical andvaginal pathology.
2. Patients with systemic disease
   e.g.hemostatic disorders
3. Patients with pregnancy.
4. Patients on hormonal treatment for abnormal uterine bleeding.

Sample Processing

The endometrial samples sent to pathology laboratory will be analyzed. These specimens will be fixed in 10% formalin. After detailed gross examination, tissue will be processed and paraffin blocks of tissue will be made; sections will be cut and stained with hematoxylin and eosin. Slides will then be

studied under light microscopy, and findings will be entered into a master chart and correlated with clinical and other relevant information available and then statistically analysed.

Data analysis

The data was collected and entered in MS excel 2010. Different statistical analysis will be performed using R software version 4.0.2.

The one-sample Kolmogorov – Smirnov test will be employed to determine whether the data sets differed from a normal distribution or not. Normally distributed data will be analysed using parametric tests and non - normally distributed data will be analysed using non parametric tests.

Descriptive statistics will be calculated for qualitative and categorical variables. Graphical representation of the variable will be shown to understand the results clearly and to measure the association for categorical dataset will be analysed using Chi-Square test.

Independent T-test or student t-test will be applied to measure the mean difference between two groups. Correlation will be estimated to measure the strength of relationship between two or more quantitative variables.

If p value <0.05, considered as statistically significant and if p-value>0.05, then it is statistically insignificant.

RESULTS

The prospective cross-sectional study titled "Histopathological Study of Endometrial Biopsies in Abnormal Uterine Bleeding" has been conducted on 130 specimens of endometrium (endometrial biopsy) received in the Department of Pathology, Santosh Deemed to be University, Ghaziabad with the clinical diagnosis of abnormal uterine bleeding.

Table: 01: AGE WISE DISTRIBUTION OF STUDY SUBJECTS

Age groups	Frequency	Percentage
<=20 years	1	0.7
21-30 years	34	26.2
31-40 years	47	36.2
41-50 years	36	27.7
51-60 years	11	8.5
>60 years	1	0.7
Total	130	100.0

The above table illustrates the age-groups of the patients. Maximum number of cases (36.2%) belonged to the 31-40 years of age followed by (27.7%) in 41-50 years of age and (26.2%) in 21-30 years of age. The youngest patient is 19 years and the eldest is 68 years of age.

Figure 1: Graphical representation of the age-groups is shown below.

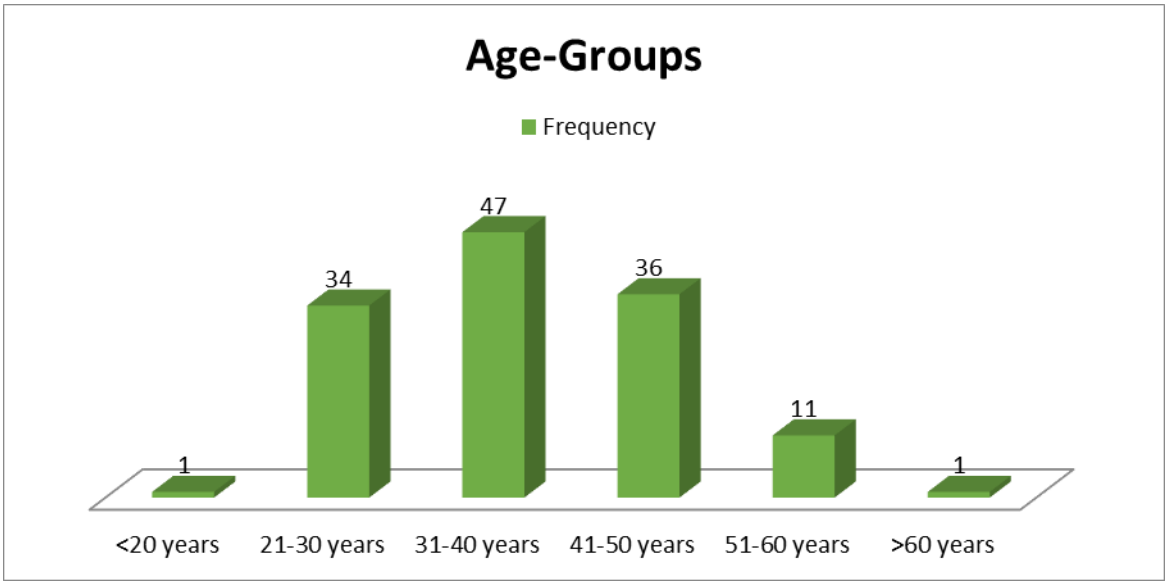


Table:02 Distribution of Parity among study subjects

Parity	Frequency	Percentage
Nulliparous	16	12.3
Multiparous (1-2)	93	71.6
Grand Multiparous (>=3)	21	16.1
Total	130	100

The above table illustrates the parity among the patients. Maximum number of cases (71.5%) are Multiparous followed by (16.1%) in grand multiparous and (12.3%) in Nulliparous.

Figure 2: Graphical representation of the parity is shown below.

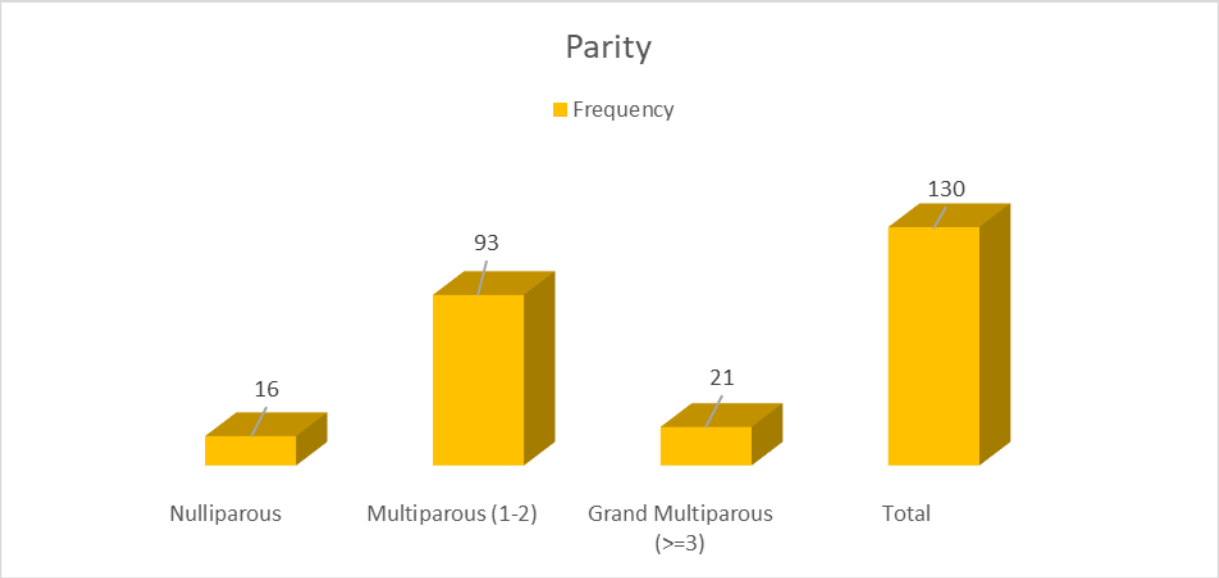


Table:03 Distribution of Bleeding patterns

Bleeding Patterns	Frequency	Percentage
Heavy bleeding (Menorrhagia)	66	50.8
Intermenstrual Bleeding (Metrorrhagia)	18	13.7
Heavy & prolonged bleeding (Menometrorrhagia)	4	3.1
Frequent menstrual bleeding (Polymenorrhoea)	11	8.5
Oligomenorrhea	7	5.4
Post-menopausal bleeding	24	18.5
Total	130	100.0

The above table illustrates the bleeding pattern of the patients. Out of 130 patients, maximum cases are in heavy bleeding (66) followed by post-menopausal bleeding (24), 18 are in Intermenstrual bleeding,Polymenorrhoea among 11 patients, Oligomenorrhoea in 7 patients and Heavy & prolonged among 4 patients.

Figure 3: Graphical Representation of the bleeding pattern is also shown below.

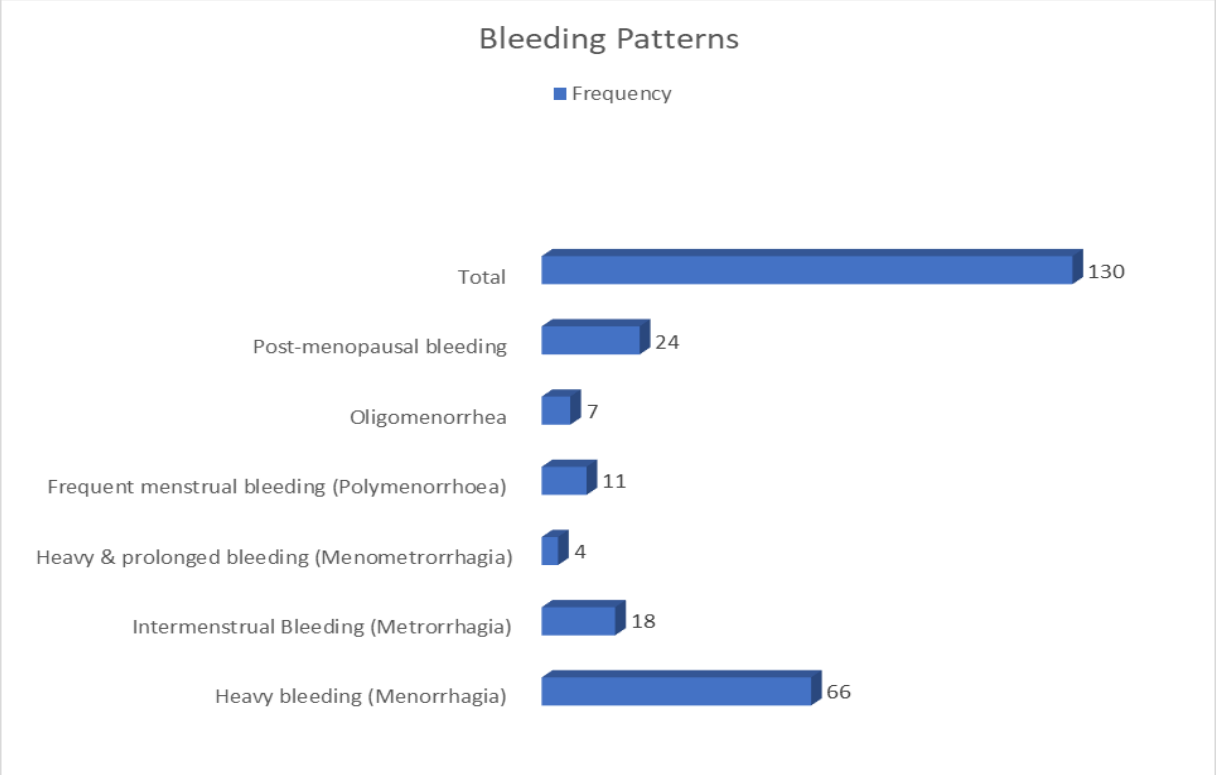


Table:04 Histopathological Diagnosis according to parity status of patients

Histopathological Diagnosis	Nulliparous	Multiparous (1-2)	Grand Multiparous (>=3)	Total	Chi-square value	p-value
Atrophic endometrium	0 (0.0%)	2 (2.15%)	2 (9.52%)	4 (3.07%)	67.59	0.023
Complex hyperplasia without atypia	1 (6.25%)	2 (2.15%)	1 (4.76%)	4 (3.07%)		
Endometrial polyp	0 (0.0%)	1 (1.07%)	0 (0.0%)	1 (0.76%)		
granulomatous endometritis	0 (0.0%)	1 (1.07%)	0 (0.0%)	1 (0.76%)		
Complex Hyperplasia with atypia	1 (6.25%)	2 (2.15%)	1 (4.76%)	4 (3.07%)		
Inflammatory lesion	0 (0.0%)	1 (1.07%)	0 (0.0%)	1 (0.76%)		
Menstrual phase	0 (0.0%)	2 (2.15%)	0 (0.0%)	2 (1.53%)		
Proliferative pattern	4 (25.0%)	34 (36.55%)	6 (28.57%)	44 (33.84%)		
Retained product of conception	1 (6.25%)	2 (2.15%)	1 (4.76%)	4 (3.07%)		
Secretory pattern	1 (6.25%)	39 (41.93%)	7 (33.33%)	47 (36.15%)		
Simple hyperplasia without atypia	8 (50.0%)	7 (7.52%)	3 (14.28%)	18 (13.84%)		
Total	16 (100.0%)	93 (100.0%)	21 (100.0%)	130 (100.0%)		

The above table illustrates the cross-tabulation betweenHistopathological diagnosis and the parity status of the patients. Maximum number of cases i.e., 47 are secretory pattern out of which 39 are Multiparous, 7 are Grand Multiparous and 1 is Nulliparous. Proliferative pattern is seen among 44 patients, out of which out of which 34 are Multiparous, 6 are Grand Multiparous and 4 are Nulliparous. Simple hyperplasia without atypia is seen among 18 patients out of which 8 are Nulliparous, 7 are Multiparous and 3 are Grand Multiparous.

Figure 4: Graphical representation of the Histopathological Diagnosis by Parity is shown below.

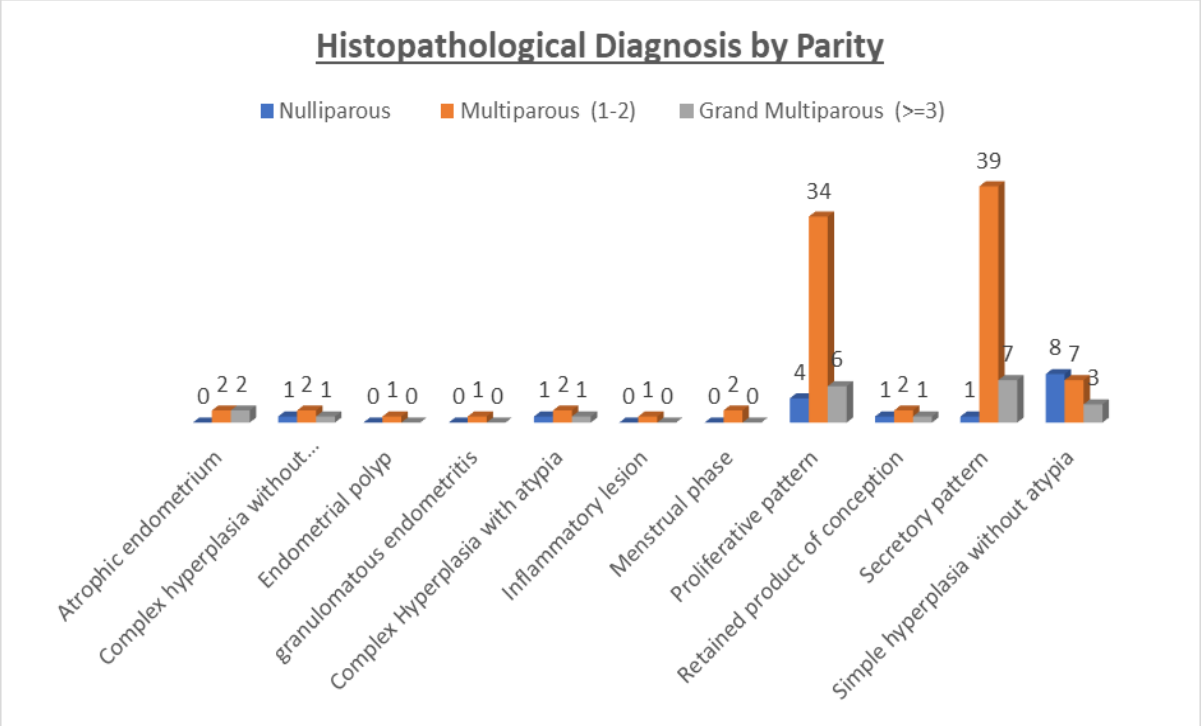


Table:05 Distribution of Histopathological Diagnosis

Histopathological Diagnosis	Frequency	Percentage
Atrophic endometrium	4	3.1
Complex hyperplasia without atypia	4	3.1
Endometrial polyp	1	0.8
Granulomatous endometritis	1	0.8
Complex Hyperplasia with atypia	4	3.1
Inflammatory lesion	1	0.8
Menstrual phase	2	1.5
Proliferative pattern	44	33.7
Retained product of conception	4	3.1
Secretory pattern	47	36.2
Simple hyperplasia without atypia	18	13.8
Total	130	100.0

Histopathologic examination of the endometrium in 130 cases revels: Secretory pattern is the most common among 47 cases (36.2%) followed by Proliferative endometrium in 44 cases (33.8%) finding in cases, Simple cystic hyperplasia without atypia is found in 18 cases (13.8%), Atrophic endometrium, Complex hyperplasia without atypia, Complex hyperplasia with atypia and Retained product of conception isfound in 4 cases (3.1%) respectively. Menstrual phase is seen in 2 patients and single case is seen inflammatory lesion, Granulomatous endometritis and Endometrial polyp respectively.

Figure 5: Graphical representation of the histopathological diagnosis

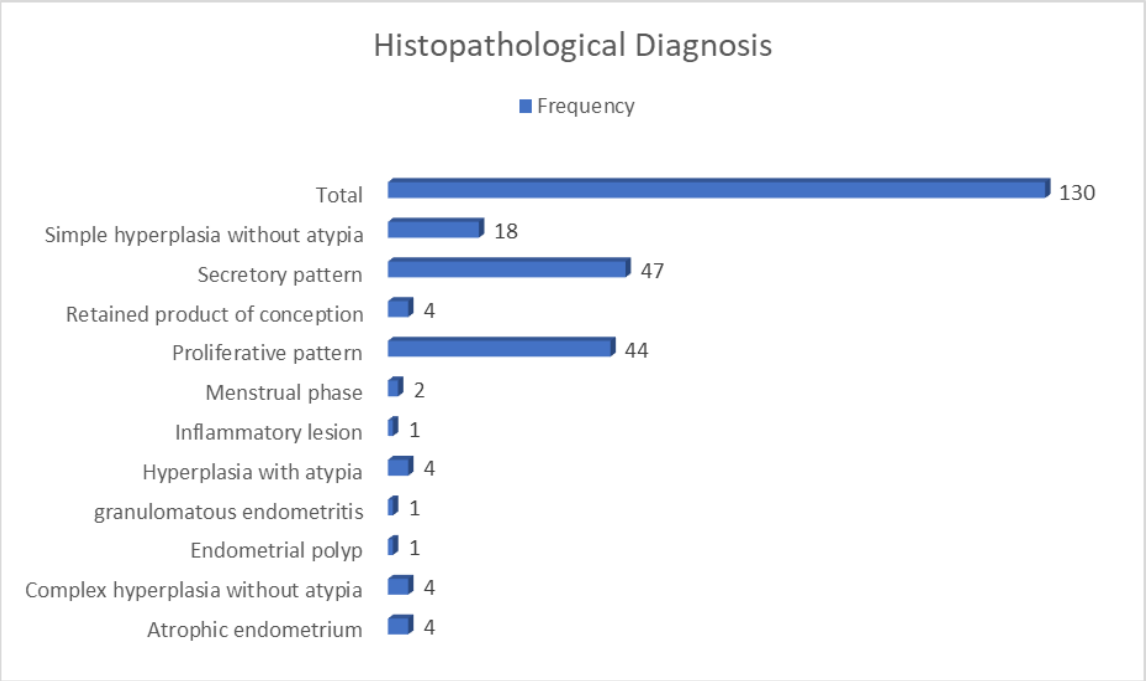


Table:06: SPLIT UP CASES OF ENDOMETRIAL HYPERPLASIA

Histopathological status	Frequency	Percentage
Complex hyperplasia without atypia	4	16.7
Simple hyperplasia without atypia	16	66.6
Complex hyperplasia with atypia	4	16.7
Total	24	100.0

The above table illustrates the hyperplasia status among patients. Out oftotal 24 cases, 16 cases are Simplex hyperplasia without atypia followed by 4 cases in each are Complex hyperplasia without atypia and Complex hyperplasia with atypia respectively.

Figure 6: Graphical representation of endometrial hyperplasia status is also shown below.

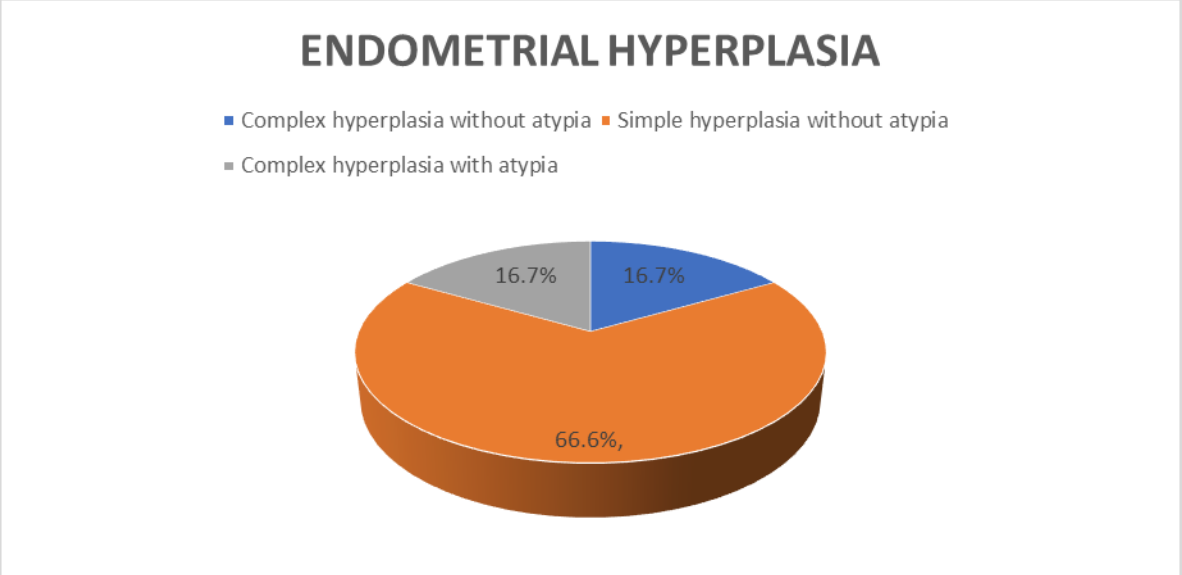


Table-7: DISTRIBUTION OF VARIOUS PATTERNS IN PREMENOPAUSAL BLEEDING GROUP

Histopathological status	Frequency	Percentage
Atrophic endometrium	2	2.1
Endometrial polyp	3	3.2
Granulomatous endometritis	2	2.1
Proliferative pattern	40	42.1
Secretory pattern	44	46.3
Simple endometrial hyperplasia without atypia	4	4.2
Total	95	100

The above table shows that out of total 95 cases, 44 cases are secretory pattern, Proliferative pattern is seen among 40 patients, Simple endometrial hyperplasia without atypia is seen among 4 patients, Atrophic endometrium and Granulomatous endometritis are seen in 2 patients each and Endometrial polyp are seen in 3 patients in premenopausal bleeding group (age).

Figure 7: Graphical representation of various patterns in premenopausal bleeding group is also shown below.

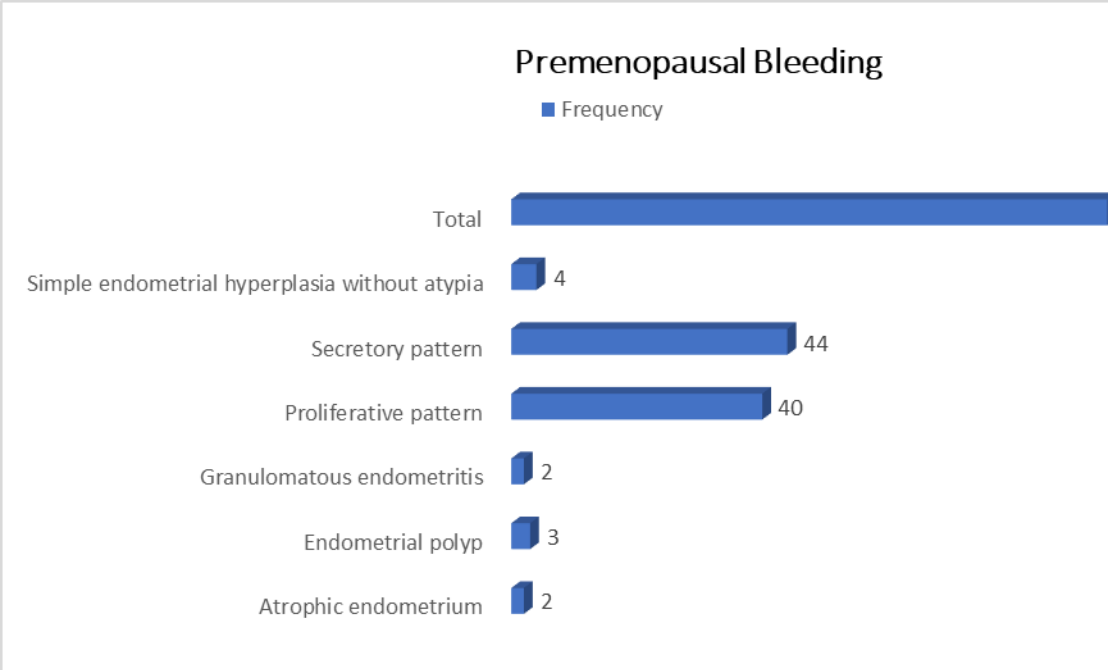


Table-8: DISTRIBUTION OF VARIOUS ENDOMETRIAL PATTERNS IN POSTMENOPAUSAL BLEEDING GROUP

Histopathological status	Frequency	Percentage
Atrophic endometrium	2	5.7
Endometrial polyp	4	11.4
Granulomatous endometritis	3	8.6
Complex hyperplasia without atypia	4	11.4
Simplex hyperplasia with atypia	16	45.8
Complex hyperplasia with atypia	4	11.4
Secretory pattern	2	5.7
Total	35	100

The above table shows that out of total 35 cases, 16 cases are Simplex hyperplasia with atypia followed by 4 cases are Granulomatous endometritis, Complex hyperplasia without atypia and Complex hyperplasia with atypia respectively. Endometrial polyp is in 3 cases, secretory pattern and atrophic endometrium are in 2 cases each

Figure 8: Graphical representation of endometrial patterns in postmenopausal group.

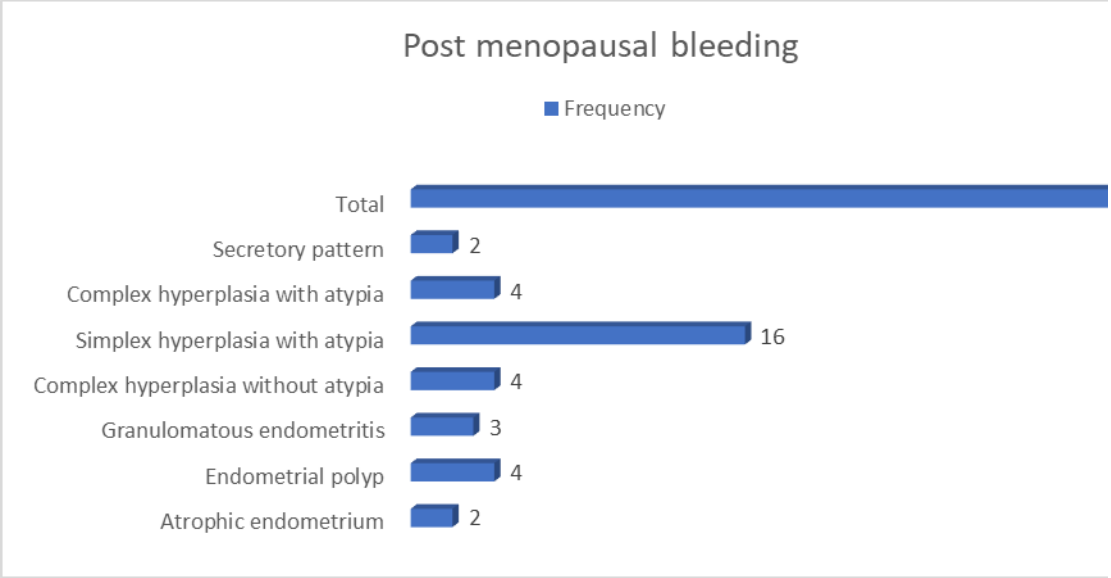


Table9: ASSOCIATION OF AGE WITH NDOMETRIAL PATTERNS

Histopathologic alDiagnosis	Age-groups						Total	Chi-square Value	p-value
	<20 years	21-30 years	31-40 years	41-50 years	51-60 years	>60 years			
Atrophic endometrium	0	0	0	3	1	0	4	91.04	0.010
	0.0%	0.0%	0.0%	8.3%	9.1%	0.0%	3.1%		
Complex hyperplasia without atypia	0	0	4	0	0	0	4		
	0.0%	0.0%	8.5%	0.0%	0.0%	0.0%	3.1%		
Endometrial polyp	0	0	1	0	0	0	1		
	0.0%	0.0%	2.1%	0.0%	0.0%	0.0%	.8%		
Granulomatous endometritis	0	1	0	0	0	0	1		
	0.0%	2.9%	0.0%	0.0%	0.0%	0.0%	.8%		
Complex Hyperplasia with atypia	0	0	2	2	0	0	4		
	0.0%	0.0%	4.3%	5.6%	0.0%	0.0%	3.1%		
Inflammatory lesion	0	0	0	0	1	0	1		
	0.0%	0.0%	0.0%	0.0%	9.1%	0.0%	.8%		
Menstrual phase	0	0	2	0	0	0	2		
	0.0%	0.0%	4.3%	0.0%	0.0%	0.0%	1.5%		
Proliferative pattern	0	11	16	15	2	0	44		
	0.0%	32.4%	34.0%	41.7%	18.2%	0.0%	33.8%		
Retained productof conception	1	1	0	2	0	0	4		
	100.0%	2.9%	0.0%	5.6%	0.0%	0.0%	3.1%		
Secretory pattern	0	19	18	7	3	0	47		
	0.0%	55.9%	38.3%	19.4%	27.3%	0.0%	36.2%		
Simple hyperplasia without atypia	0	2	4	7	4	1	18		
	0.0%	5.9%	8.5%	19.4%	36.4%	100.0%	13.8%		
Total	1	34	47	36	11	1	130		
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%		

The above table illustrates the association between the age-groups and the histopathological status among cases with abnormal uterine bleeding. It is found that maximum number ofcases in Secretory pattern as 47 cases (36.2%) followed by Proliferative endometrium in 44 cases (33.8%) finding in cases with abnormal uterine bleeding.

Maximum number of cases of Secretory Pattern lies between 21-30 years and 31-40 years.

It is found that association between age-group and histopathological status is highly statistically significant (p-value<0.05).

<u>Figure 9:</u> Proliferative Phase showing Tubular Glands lined by Pseudostratified Epithelium surrounded by Cellular Stroma

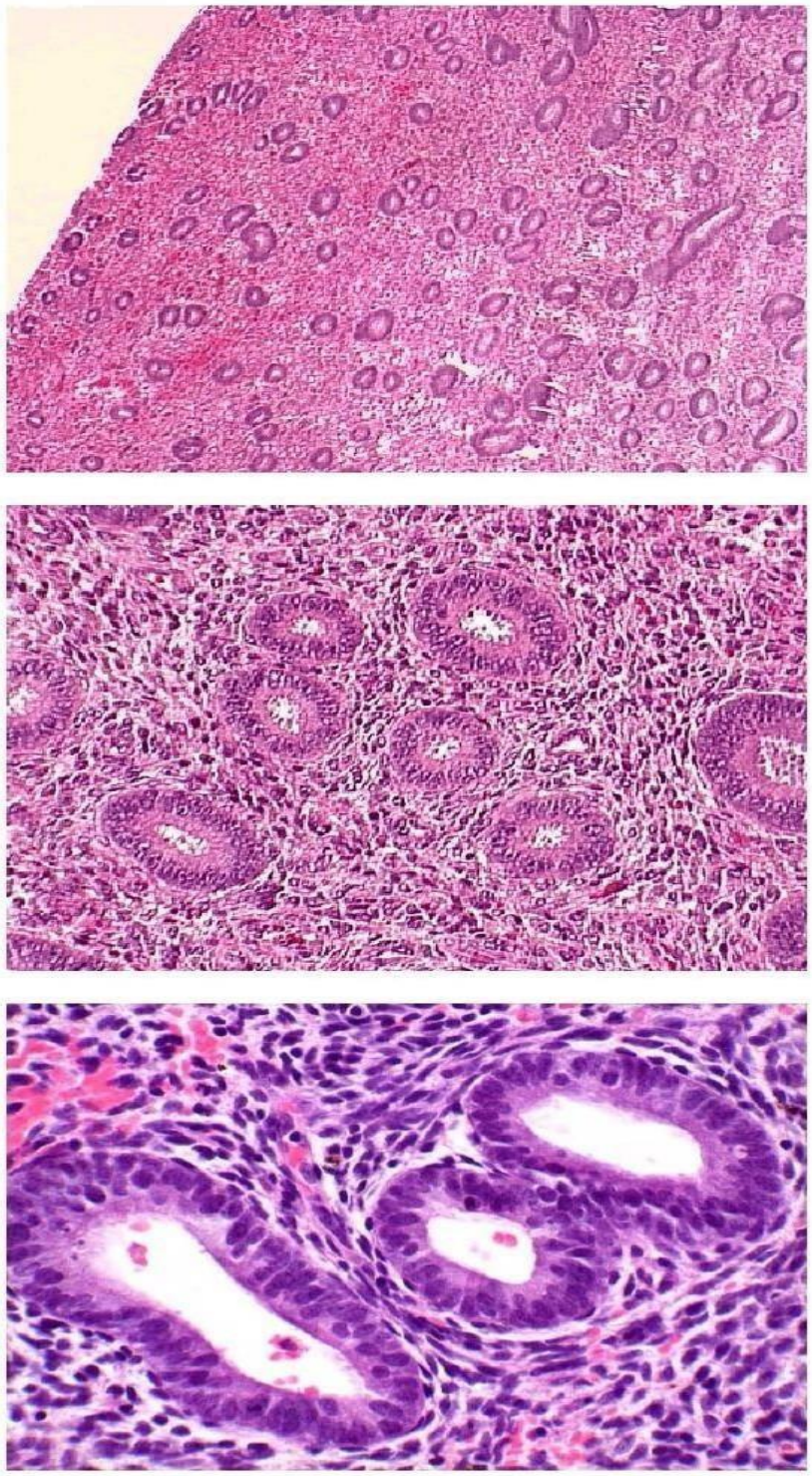
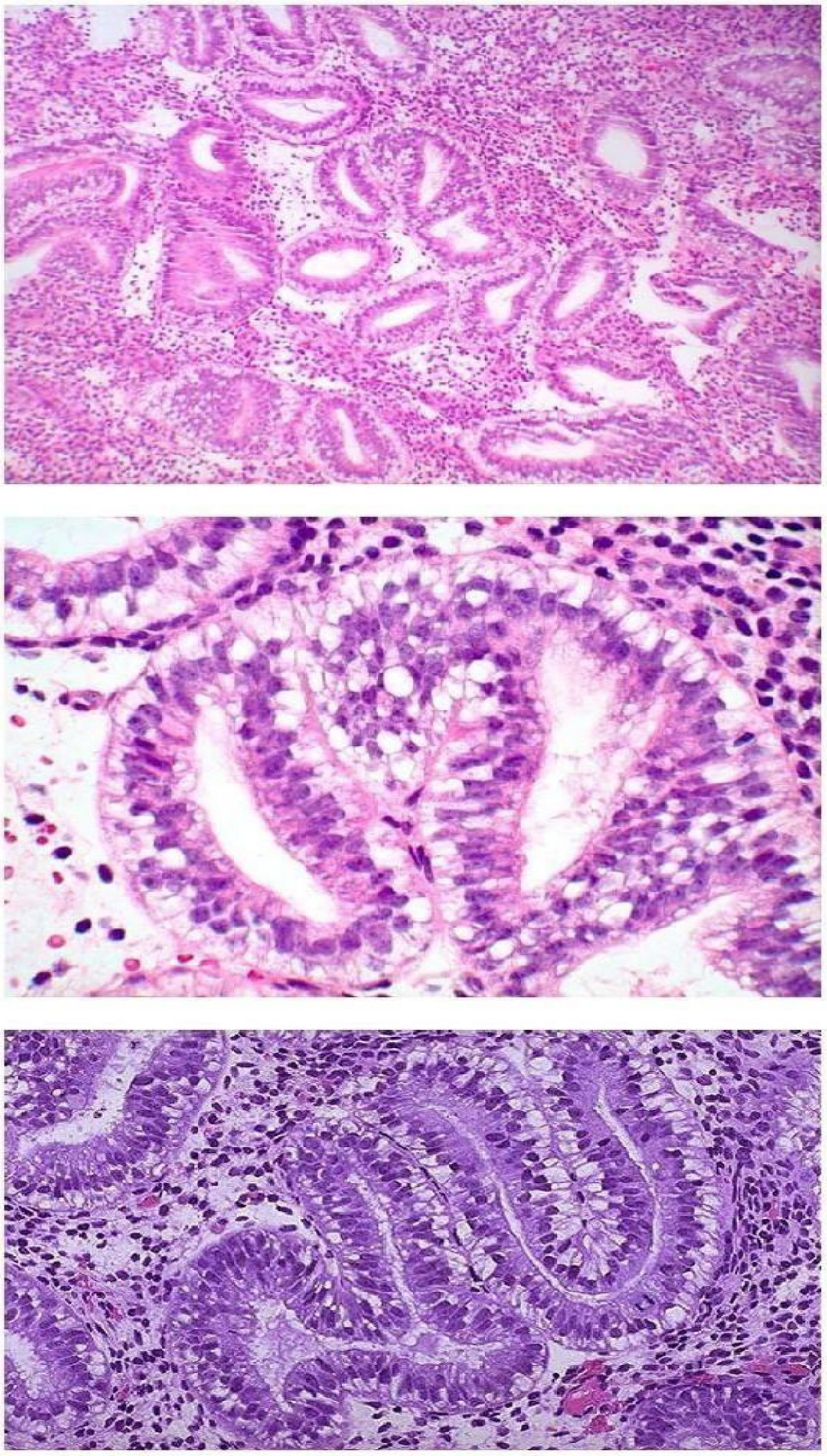
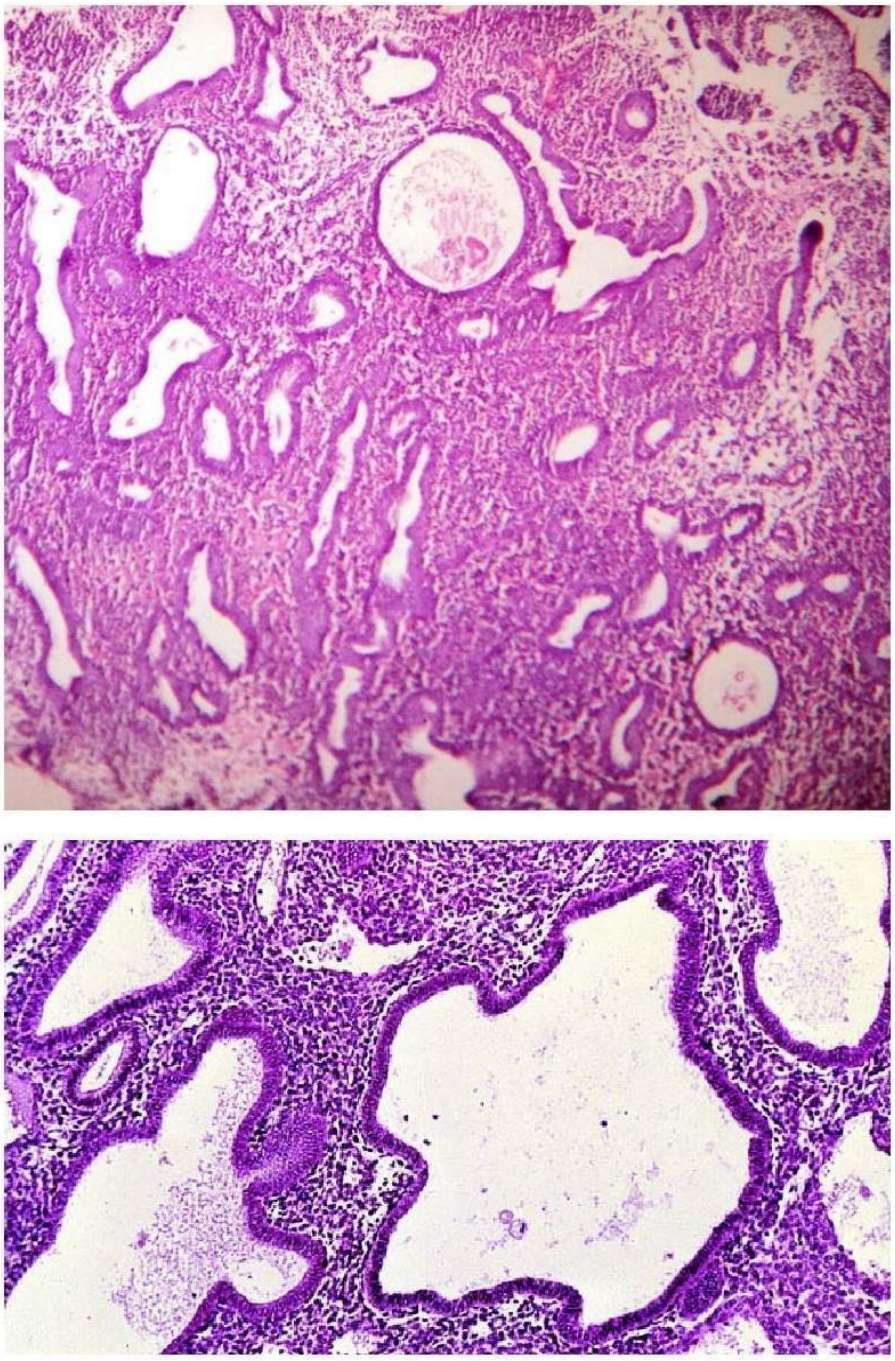


Figure 10: Secretory Phase with tortuous glands showing Subnuclear Vacuolation and Oedematous Stroma



<u>Figure 11:</u> Simple hyperplasia without Atypia with Large Cystically dilated glands against compact stroma



<u>Figure 12:</u> Complex Hyperplasia without Atypia with Overcrowding of glands, Complex Glandulararchitecture without nuclear Atypia

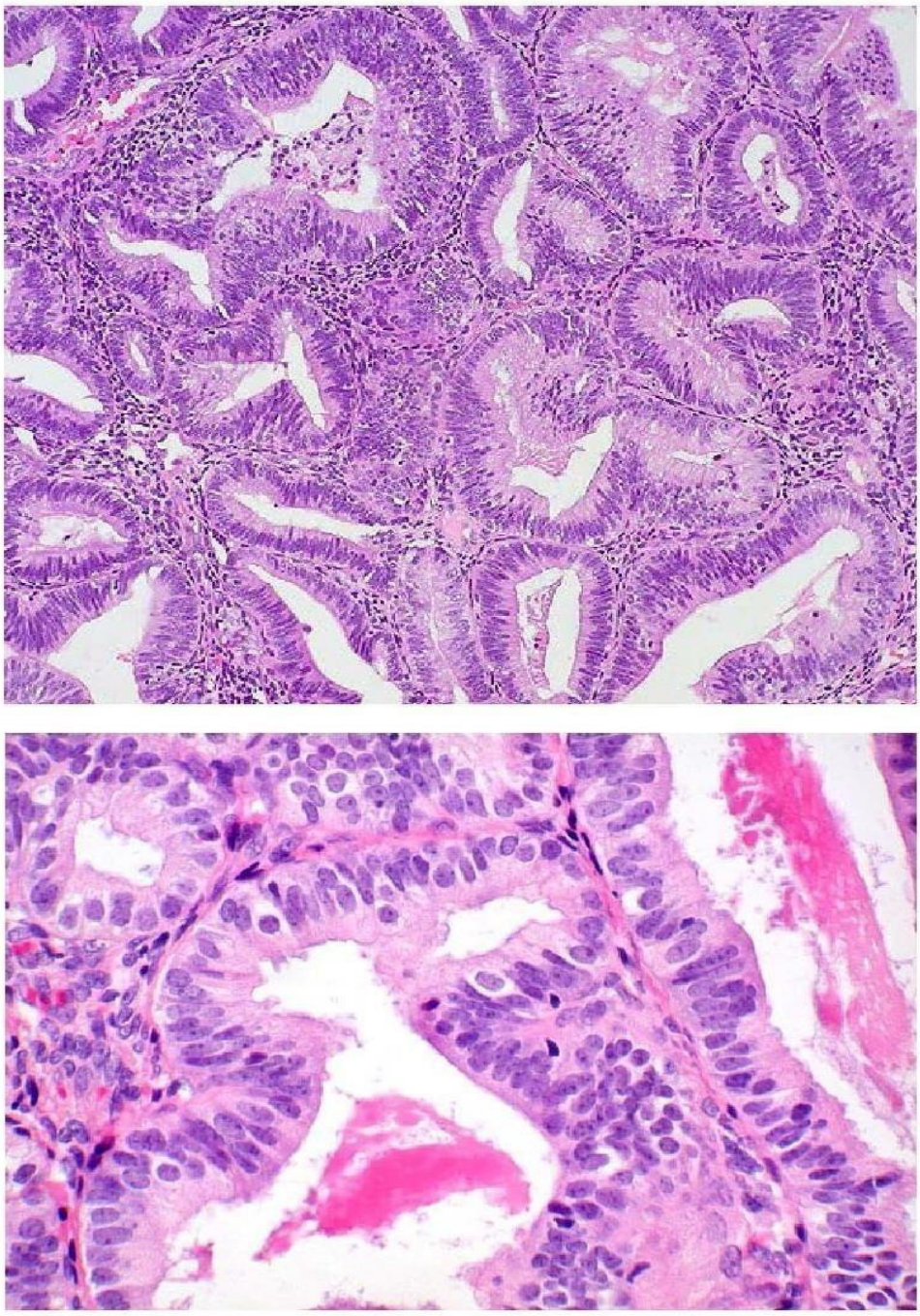
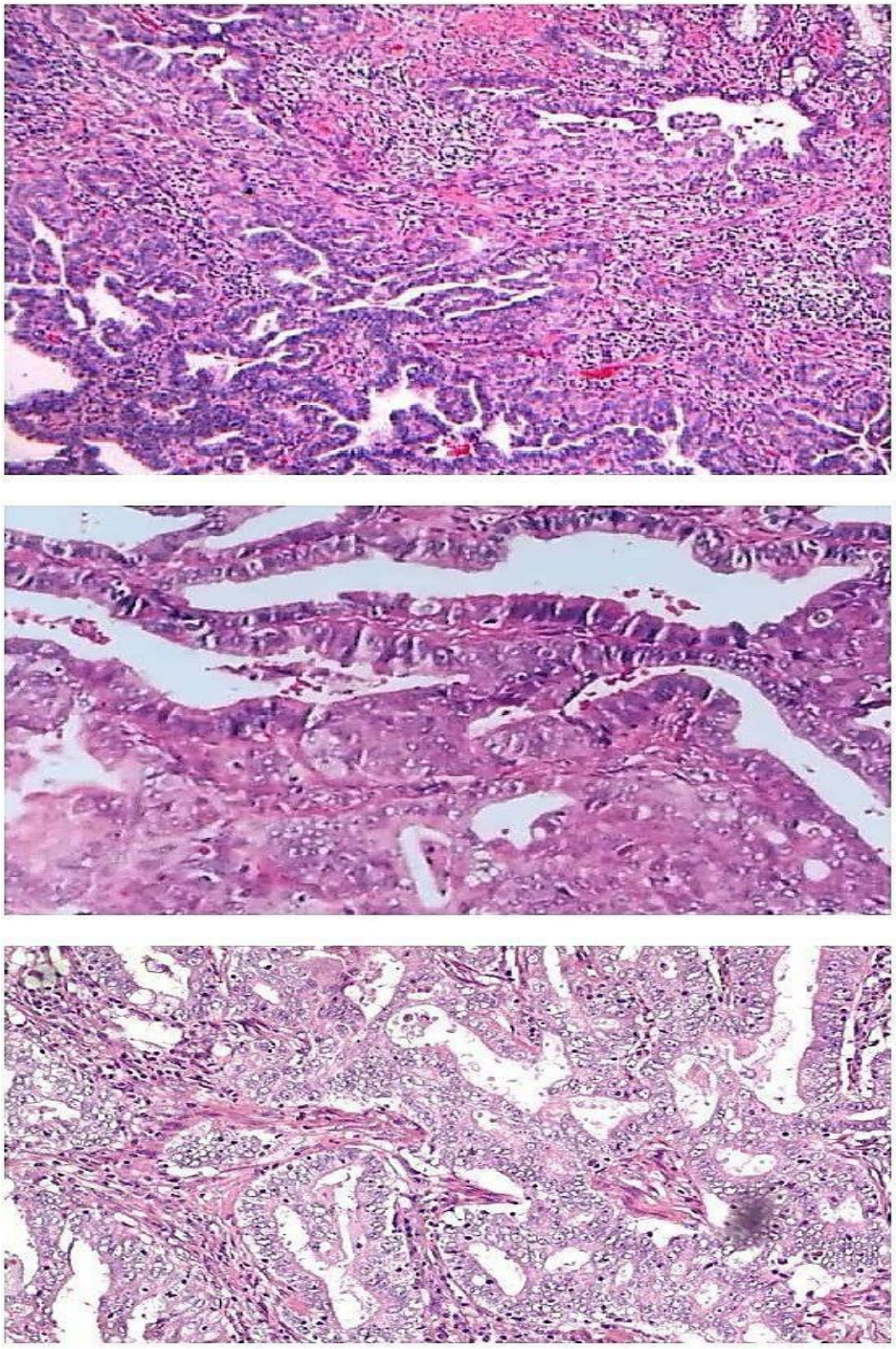
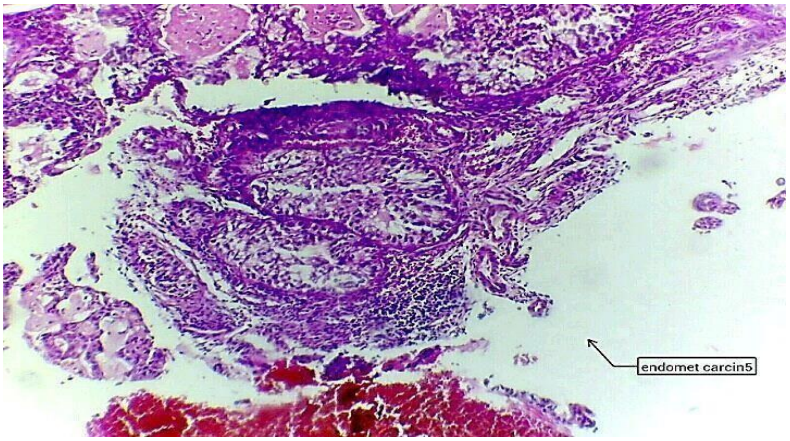
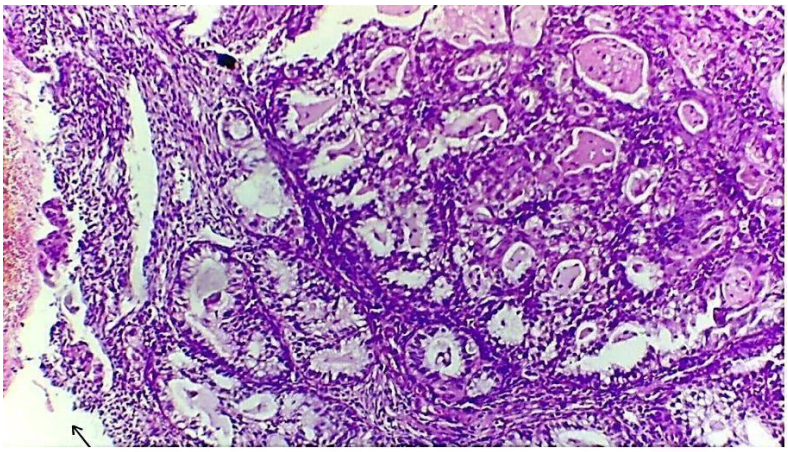


Figure 13: **Endometrial Adenocarcinoma showing overcrowding of glands, intraglandular bridging,papillary projections with nuclear Atypia and mitosis**

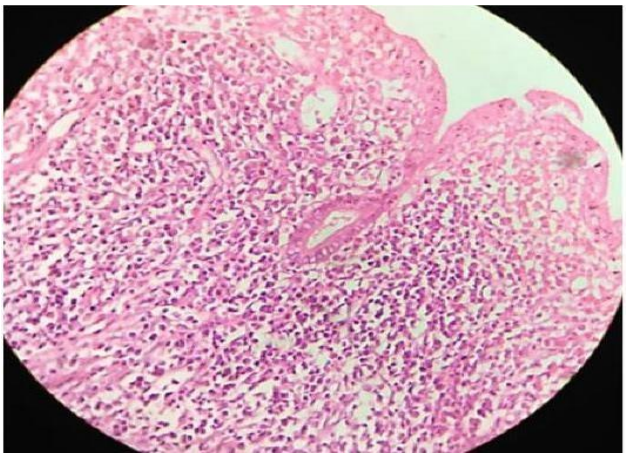
Figure 14: **Endometroid Carcinoma – Secretory variant of Uterus**







<u>Figure 15:</u> Chronic Endometritis showing plasma cells in stroma



DISCUSSION

Abnormal uterine bleeding continues to be one of the most common and perplexing problems in Gynaecological practice. It may present at any age between puberty and menopause. It may be associated with various kinds of histopathological findings in the endometrium.

In the current study, the incidence of AUB was observed in age group between 31-40 years ofage. The findings of our study are consistent with several other studies reported earlier. [32-34]. However, several other studies have also reported maximum incidence in 21-30 years age group [35-36]. Considering these discrepant observations, one may conclude that, any age after menarche is not exempt from AUB. The highest incidence of AUB was seen in the reproductive age group (21-40 years) in the present study (60.5%) which is in concordance with the results of the studies by Sutherland (58.5%) and Mehrotra et al (71.3%) [37,38].

Our study results have shown that maximum number of cases (71.5%) were Multiparous followed by (16.1%) in grand multiparous and (12.3%) in Nulliparous. Furthermore, proliferative pattern was seen among 44 patients, out of which out of which 34 were Multiparous, 6 were Grand Multiparous and 4 were Nulliparous. Simple hyperplasia without atypia was seen among 18 patients out of which 8 were Nulliparous, 7 were Multiparous and3 were Grand Multiparous.

Out of 130 patients enrolled in our study, maximum cases were in heavy bleeding (66) followed by post-menopausal bleeding (24), 18 were in Intermenstrual bleeding, Polymenorrhoea among 11 patients, Oligomenorrhoea in 7 patients and Heavy & prolonged among 4 patients.

Histopathologic examination of the endometrium in 130 cases revealed: Secretory pattern wasthe most common among 47 cases (36.2%) followed by Proliferative endometrium in 44 cases(33.8%) finding in cases, Simple cystic hyperplasia without atypia was found in 18 cases (13.8%), Atrophic endometrium, Complex hyperplasia without atypia, Complex hyperplasia with atypia and Retained product of conception was found in 4 cases (3.1%) respectively. Menstrual phase was seen in 2 patients and single case was seen inflammatory lesion, S Granulomatous endometritis and Endometrial polyp respectively. Our current findings are veryclose to the observations made by Abdullah et al who also reported proliferative endometrium as the most common endometrial pattern in their study (37.1%).

Endometrial carcinoma was diagnosed in 3.35%, 13.04% and 18% cases of endometrial carcinoma respectively in the postmenopausal bleeding group. Disordered endometrium was reported by Dadhania et al in 8%,8% and 6% cases of postmenopausal bleeding group [40].

Table --: Comparison of the number and percentage of patients diagnosed with proliferative pattern and secretory patterns based on the results observed in the current study with few similar earlier studies.

Histopathological Diagnosis	**Present Study**		**Ebrahim Soleymani etal.,(44)**		**Khanna & Sudha(45)**		**Sajitha et al.,(46)**	
	No	**%**	**No**	**%**	**No**	**%**	**No**	**%**
Proliferative pattern	44	33.8	70	35.0	34	42.5	26	16.7
Secretory pattern	47	36.2	53	26.5	19	23.7	19	12.8
Total	130		200		80		156	

In our study, out of all the cases the most predominant pattern observed from the results are the secretory pattern followed by the proliferative endometrium in the age groups of 21-30 years and 31-40 years respectively.

SUMMARY

The current study was conducted to assess the histopathology of endometrium for identifying the causes of abnormal uterine bleeding among different age groups and to find out endometrial carcinoma in perimenopausal and postmenopausal women. A prospective observational cross-sectional study was conducted among 130 specimens received in the Department of Pathology, Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh. The endometrial samples sent to pathology laboratory was analysed. These specimens were fixed in 10% formalin. After detailed gross examination, tissue was processed and paraffin blocks of tissue were made; sections were cut and stained with haematoxylin and eosin. Slides were then be studied under light microscopy, and findings were entered into a master chart and correlated with clinical and other relevant information available and then statistically analysed.

Maximum number of cases (36.2%) belonged to the 31-40 years of age followed by (27.7%) in 41-50 years of age and (26.2%) in 21-30 years of age. The youngest patient is 19 years andthe eldest is 68 years of age. Maximum number of cases (71.5%) are Multiparous followedby (16.1%) in grand multiparous and (12.3%) in Nulliparous. Maximum number of cases (47)are secretory pattern out of which 39 are Multiparous, 7 are Grand Multiparous and 1 is Nulliparous. Proliferative pattern is seen among 44 patients, out of which out of which 34 are Multiparous, 6 are Grand Multiparous and 4 are Nulliparous. Simple hyperplasia without atypia is seen among 18 patients out of which 8 are Nulliparous, 7 are Multiparous and 3 are Grand Multiparous. Out of 130 patients, maximum cases are in heavy bleeding (66) followed by post-menopausal bleeding (24), 18 are in Intermenstrual bleeding, Polymenorrhoea among 11 patients, Oligomenorrhoea in 7 patients and Heavy & prolonged among 4 patients.

Secretory pattern is the most common among 47 cases (36.2%) followed by Proliferative endometrium in 44 cases (33.8%) finding in cases, Simple cystic hyperplasia without atypia is found in 18 cases (13.8%), Atrophic endometrium, Complex hyperplasia without atypia, Complex hyperplasia with atypia and Retained product of conception is found in 4 cases (3.1%) respectively. Menstrual phase is seen in 2 patients and single case is seen inflammatory lesion, Granulomatous endometritis and Endometrial polyp respectively.

Out of total 24 cases, 16 cases are Simplex hyperplasia without atypia followed by 4 cases in each are Complex hyperplasia without atypia and Complex hyperplasia with atypia respectively. It is found that maximum number of cases in Secretory pattern as 47 cases (36.2%) followed by Proliferative endometrium in 44 cases (33.8%) finding in cases with abnormal uterine bleeding. Maximum number of cases of Secretory Pattern lies between 21-30 years and 31-40 years. It is found that association between age-group and histopathological status is highly statistically significant (p-value<0.05).

CONCLUSIONS

Following conclusions are drawn from the current study:

- Patients with abnormal uterine bleeding experience pre-menopausal bleeding more frequently than post-menopausal bleeding.
- Secretory endometrium followed by Proliferative pattern constitute the commonest endometrial pattern in pre-menopausal age group in patients of abnormal uterine bleeding.
- Simplex hyperplasia with atypia followed by Granulomatous endometritis is common in the post-menopausal age group in patients of abnormal uterine bleeding.
- The study concludes that histopathological findings of endometrium among patients of abnormal uterine bleeding plays a significant role in diagnosing various gynecological problems and somehow it is mandatory among patients of abnormal

uterine bleeding.

The endometrium can be studied histopathologically to identify benign lesions like disordered endometrium, atrophic endometrium, and chronic endometritis as well as malignant lesions like endometrial carcinoma and endometrial stromal sarcoma, which can have a better prognosis if detected early.

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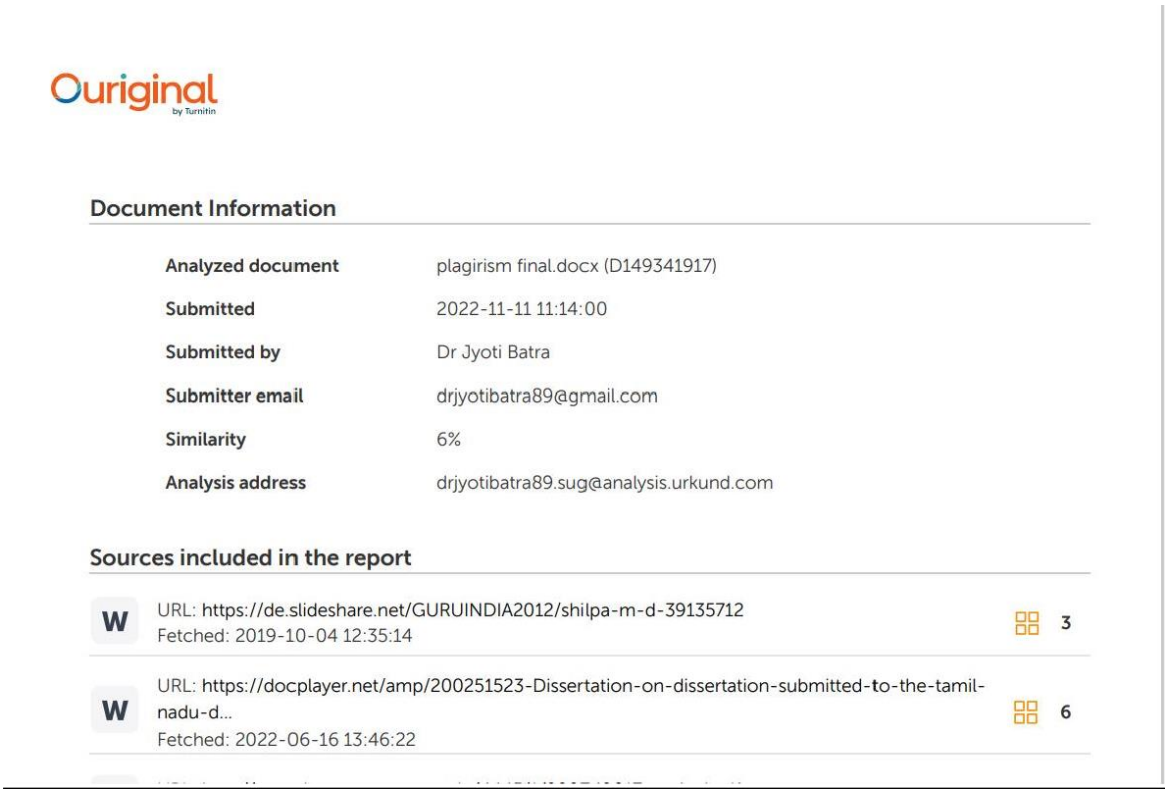
ANNEXURE I

PLAGIRISM CERTIFICATE



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ANNEXURE II

STAINING TECNIQUES

Hematoxylin and Eosin (H& E)

Procedure

1. Bring sections to water
2. Stain with Harris Hematoxylin for 2-3 minutes
3. Wash with running tap water
4. Differentiate in 1% acid alcohol
5. Wash and blue with running tap water
6. Counter stain with aqueous eosin for 2 minutes
7. Dehydrate with absolute alcohol (2-3 changes)
8. Clear with 2-3 changes of xylene
9. Mount using Dibutyl phthalate polystyrene xylene (Dpx)

Results

Nucleic acid – blue

Cytoplasm – pink

ANNEXURE III

PROFORMA

NAME:	IPNO.:	CASE NO:
AGE:	DOA:	BIOPSY NO:
OCCUPATION:	DOD:	
	WARD:	

ENDOMETRIAL BIOPSY/SCRAPINGS/D&C:

GROSS:

MICROSCOPY:

SPECIALSTAINS:

FINAL HISTOPATHOLOGICAL DIAGNOSIS

ANNEXURE IV

MASTERCHART

Sr. No.	Name	Age	OPD/IPD No.	Biopsy No.	Histopathological Diagnosis
1	Poonam	19	17048036	S440/19	Retained Product Of Conception
2	Shabnam	48	17044636	S434/19	Proliferative Pattern
3	Shalini	30	17044607	S430/19	Proliferative Pattern
4	Shivani	21	17018792	S482/19	Secretory Pattern
5	Nainwati	36	17043194	S427/19	Menstrual Phase
6	Lalita	34	17020144	S419/19	Secretory Pattern
7	Hussain Jahu	46	17040501	S417/19	Secretory Pattern
8	Pooja	46	17024120	S396/19	Secretory Pattern
9	Usha	34	17014263	S394/19	Proliferative Pattern
10	Lalita	53	17030925	S393/19	Proliferative Pattern
11	Kusum	28	17027119	S379/19	Secretory Pattern
12	Sona	31	17011911	S370/19	Secretory Pattern
13	Anshu	51	17023490	S368/19	Secretory Pattern
14	Manju	40	17022894	S363/19	Menstrual Phase
15	Suman	39	17022514	S361/19	Simple Hyperplasia Without Atypia
16	Anika	27	17021198	S360/19	Simple Hyperplasia Without Atypia
17	Neetu	30	17001311	S358/19	Secretory Pattern
18	Guddi	38	17016645	S353/19	Proliferative Pattern
19	Sarojni	30	17009581	S335/19	Proliferative Pattern
20	Shalini	40	17007474	S330/19	Secretory Pattern
21	Nagma	38	17002640	S323/19	Simple Hyperplasia Without Atypia
22	Sudha	49	17002348	S319/19	Simple Hyperplasia Without Atypia
23	Iram	34	17001785	S319/19	Secretory Pattern
24	Ram	52	29001793	S315/19	Secretory Pattern

25	Bharti	35	190918015	S309/19	Secretory Pattern
26	Awnesh	68	190917004	S307/19	Simple Hyperplasia Without Atypia
27	Kavita	50	190916021	S305/19	Simple Hyperplasia Without Atypia
28	Pinki	35	190909080	S298/19	Secretory Pattern
29	Rabhma	33	190913047	S297/19	Secretory Pattern
30	Sunita	42	190909022	S288/19	Simple Hyperplasia Without Atypia
31	Bala Devi	48	190909009	S280/19	Proliferative Pattern
32	Pooja	24	190821006	S263/19	Secretory Pattern
33	Monika	42	190820004	S261/19	Proliferative Pattern
34	Mamta	41	190813048	S250/19	Simple Hyperplasia Without Atypia
35	Preeti	26	190806090	S242/19	Secretory Pattern
36	Sunita	23	190731093	S234/19	Secretory Pattern
37	Saje Biwi	38	190731009	S233/19	Proliferative Pattern
38	Archana	30	190727013	S231/19	Granulomatous Endometritis
39	Roopender	30	190726009	S229/19	Secretory Pattern
40	Mamta	24	190723141	S226/19	Retained Product Of Conception
41	Raj Kumari	40	190720068	S221/19	Secretory Pattern
42	Roopa	30	190718024	S220/19	Proliferative Pattern
43	Seema	24	190715003	S231/19	Proliferative Pattern
44	Babli	22	1907090283	S210/19	Secretory Pattern
45	Nikki	28	190713030	S209/19	Proliferative Pattern
46	Manju	55	190703055	S202/19	Simple Hyperplasia Without Atypia
47	Vandana	28	190701035	S198/19	Proliferative Pattern
48	Kusum	30	17204312	S270/20	Secretory Pattern
49	Asshi	24	17061961	S82/20	Secretory Pattern
50	Manju	52	17069179	S78/20	Secretory Pattern
51	Pooja	36	17060785	S51/20	Secretory Pattern
52	Omwati	30	17094338	S225/21	Secretory Pattern
53	Babita	40	17104008	S194/21	Secretory Pattern
54	Shanti	47	17114011	S162/21	Simple Hyperplasia Without Atypia

55	Rajni	45	13009753	S145/21	Proliferative Pattern
56	Pooja	36	17098752	S117/21	Complex Hyperplasia Without Atypia
57	Kalpna	41	17098527	S98/21	Simple Hyperplasia Without Atypia
58	Mamta	39	17091918	S59/21	Proliferative Pattern
59	Mumta	22	17085609	S50/21	Secretory Pattern
60	Jayant	25	17089446	S41/21	Secretory Pattern
61	Rukaiya	25	17194356	S277/22	Proliferative Pattern
62	Kajal Devi	25	17190110	S240/22	Proliferative Pattern
63	Anita	45	17128279	S239/22	Proliferative Pattern
64	Sarla	38	17201027	S229/22	Proliferative Pattern
65	Asha Devi	46	17200882	S223/22	Secretory Pattern
66	Adesh	55	17200403	S216/22	Proliferative Pattern
67	Laxmi	35	17199038	S199/22	Secretory Pattern
68	Meena	42	13011886	S198/22	Hyperplasia With Atypia
69	Seema	32	17147561	S173/22	Endometrial Polyp
70	Mantoriya Devi	60	13012117	S169/22	Inflammatory Lesion
71	Shashi Agarwal	59	17136107	S158/22	Simple Hyperplasia Without Atypia
72	Sunita	50	17187085	S155/22	Proliferative Pattern
73	Anjali Gupta	35	17196022	S156/22	Secretory Pattern
74	Sapna	35	17184779	S152/22	Hyperplasia With Atypia
75	Kaushalya	28	17186692	S123/22	Simple Hyperplasia Without Atypia
76	Heena	45	17154834	S116/22	Secretory Pattern
77	Ruchi	41	17127162	S112/22	Simple Hyperplasia Without Atypia
78	Kusum	38	17184679	S107/22	Proliferative Pattern
79	Sunita	45	17182865	S100/22	Secretory Pattern
80	Suman	42	17189392	S98/22	Hyperplasia With Atypia
81	Rekha	38	17186733	S93/22	Proliferative Pattern
82	Vidhya	59	17178814	S92/22	Simple Hyperplasia Without Atypia
83	Ravita	36	17181283	S90/22	Secretory Pattern

84	Neetu Kumari	24	17171388	S89/22	Proliferative Pattern
85	Seema	23	17176110	S55/22	Secretory Pattern
86	Laxmi	36	17101120	S47/22	Proliferative Pattern
87	Kavita	38	17166127	S38/22	Proliferative Pattern
88	Meera	40	13011410	S33/22	Secretory Pattern
89	Klipa	44	17088082	S30/22	Proliferative Pattern
90	Sayena	45	17169970	S28/22	Retained Product Of Conception
91	Meeta	36	17164112	S26/22	Proliferative Pattern
92	Neelam	30	17160015	S17/22	Proliferative Pattern
93	Sangeeta	37	17158344	S003/22	Complex Hyperplasia Without Atypia
94	Nishu	32	17199771	S311/22	Secretory Pattern
95	Meena Raj	48	17180723	S319/22	Secretory Pattern
96	Monika	24	17195458	S288/22	Secretory Pattern
97	Geeta	45	17195493	S354/22	Proliferative Pattern
98	Poonam	48	17203981	S315/22	Proliferative Pattern
99	Sheetal	40	17217150	S432/22	Proliferative Pattern
100	Rajiv	41	19218336	S423/22	Proliferative Pattern
101	Preeti	42	17214846	S414/22	Proliferative Pattern
102	Dolly	30	17216071	S384/22	Secretory Pattern
103	Satyawati Devi	58	17214982	S377/22	Simple Hyperplasia Without Atypia
104	Suman	35	17212519	S368/22	Proliferative Pattern
105	Kanchana	53	18145172	S811/22	Atrophic Endometrium
106	Jayalakshmi	38	17293063	S828/22	Simple Hyperplasia Without Atypia
107	Lakshmi	44	19342472	S850/22	Atrophic Endometrium
108	Jabeen	40	18264166	S856/22	Secretory Pattern
109	Sagai Mary	45	17916825	S922/22	Secretory Pattern
110	Kurshid	48	19356699	S921/22	Atrophic Endometrium
111	Suma Shekhar	45	17642053	S941/22	Atrophic Endometrium
112	Rubina Banu	30	17634237	S889/22	Secretory Pattern
113	Rajamma	30	17410568	S956/22	Secretory Pattern
114	Gajalakshmi	45	17397444	S210/22	Proliferative Pattern
115	Devamma	45	17816512	S260/22	Proliferative Pattern

116	Geeta	38	18663275	S321/22	Hyperplasia With Atypia
117	Zainab	38	17658762	S365/22	Complex Hyperplasia Without Atypia
118	Rohini	42	17561541	S410/22	Proliferative Pattern
119	Sharada	38	18364788	S401/22	Proliferative Pattern
120	Nageena Taj	40	19171120	S478/22	Simple Hyperplasia Without Atypia
121	Jyoti Kumara	39	19326087	S178/22	Complex Hyperplasia Without Atypia
122	Swapna	35	18050323	S657/22	Proliferative Pattern
123	Ravita	36	17181283	S90/22	Secretory Pattern
124	Neetu Kumari	24	17171388	S89/22	Proliferative Pattern
125	Seema	23	17176110	S55/22	Secretory Pattern
126	Laxmi	36	17101120	S47/22	Proliferative Pattern
127	Kavita	38	17166127	S38/22	Proliferative Pattern
128	Meera	40	13011410	S33/22	Secretory Pattern
129	Klipa	44	17088082	S30/22	Proliferative Pattern
130	Sayena	45	17169970	S28/22	Retained Product Of Conception